PLANT PROTEINS IN CHILD FEEDING

R. F. A. DEAN

L-9C;32
NS3

2884

PREFACE

ONE of the most important roles played by cow's milk in the feeding of children is to supplement the rest of the diet. Children who have enough milk are usually healthy and grow well. There are many parts of the world, however, where milk is scarce, and the development of other foods which would have the same general effects as milk, but which could be easily and cheaply prepared from locally available raw materials, would therefore be of great practical value. The urgency of this need has led in recent years to an increasing consideration of the possibility of using combinations of plant products for this purpose.

After the food shortage in Italy in 1944, when mixtures of soya flour and malted cereals proved useful as emergency supplements for children, the United Nations Relief and Rehabilitation Administration asked Dame Harriette Chick of the Lister Institute of Preventive Medicine to investigate fully their nutritive value in animal experiments. The results were promising and showed the need for carefully controlled clinical trials to decide whether children would thrive on such mixtures as a regular part of their diet. While a Medical Research Council team under the direction of Professor R. A. McCance was studying undernutrition in Germany from 1946 to 1949, Dr. R. F. A. Dean, one of its members, was able to investigate the value of plant mixtures as additions to the diets of schoolchildren and children living in orphanages.

The children were of all ages up to 11 years, including many between 6 months and 2 years old, an age group which it is particularly difficult to feed well without milk. The diets contained little animal protein, and the general plan of the investigation was to give supplements of cow's milk or of cereal and soya mixtures and to compare their effects on the children's growth and health. Although many difficulties became apparent during the course of the work, the excellent growth of most of the children suggested that it may ultimately be possible to provide mixtures of foods entirely of plant origin rivalling milk in nutritive value. Dr. Dean recommends the examination of other sources of protein indigenous to the areas where children's diets are poor, and the Council, with the co-operation of the Government of Uganda, have recently established a Research Group at Kampala, Uganda, under his direction, to study this and other problems of infant nutrition.

The planning and results of the trials in Germany are described in Part II of this Report. They are preceded by a review of some of the many problems related to the use of plant proteins, special attention being given to the child's nutritional needs and to some of the possible ways of satisfying them. The Council are glad to publish this Report in their series, for they believe that the results described will be of interest to those concerned with the practical and economic aspects of feeding children, particularly under conditions in which milk and other sources of animal protein are inadequate or unacceptable.

MEDICAL RESEARCH COUNCIL,   *June* 22, 1953
    38 Old Queen Street,
        London, S.W.1.

CONTENTS

PART I: A DISCUSSION OF THE PRINCIPLES, A SURVEY OF PAST EXPERIENCE, AND AN ACCOUNT OF SOME COMPLICATING FACTORS IN ASSESSING THE BIOLOGICAL VALUE OF PROTEINS

CONTENTS

PART II: A DESCRIPTION OF SOME EXPERIMENTS IN THE USE OF PLANT PREPARATIONS

CONTENTS

PLANT PROTEINS IN CHILD FEEDING

by

R. F. A. DEAN, Ph.D., M.R.C.S.

PART I: A DISCUSSION OF THE PRINCIPLES, A SURVEY OF PAST EXPERIENCE, AND AN ACCOUNT OF SOME COMPLICATING FACTORS IN ASSESSING THE BIOLOGICAL VALUE OF PROTEINS

Introduction

THE early history of the chemical investigation of living material consisted largely of attempts to show that those substances which Mulder (1839) called proteins were the same whether they were derived from animal or plant sources. It was thought reasonable that if plants were eaten by animals, the intact proteins should become part of the animal body. The process seemed simple, obvious and economical.

The theory of the essential similarity of all proteins was discarded when it was realized that reliance on elementary composition had obscured more subtle differences. As more and more differences were brought to light, it seemed increasingly justifiable to divide proteins according to their origin; animal proteins became superior or "first class", and plant proteins inferior or "second class". It is now generally agreed that this concept should be abandoned in its turn, because it appears that nearly all the proteins of living matter, whatever their origin, consist of various arrangements of about 20 different amino-acids. It appears also that the proportions in which the amino-acids occur in the proteins are remarkable as much for their similarities as for their differences (Block and Mitchell, 1946–7). The possibility of exploiting the similarities between the amino-acid composition of the proteins of milks and of plants forms the basis of this Report.

The Quantitative Relation between Protein and other Constituents in the Diets of Young Children

Any investigation of the possibilities of using plant proteins to feed young children should perhaps begin by considering the amount of protein which is required.

One way in which this can be found for a child in the first few months of life is by calculating the intake from human milk. The supply of breast milk does not, in practice, often exceed 700 to 800 g. daily, which contains between 8·5 and 11·0 g. protein. A woman, whose lactation was studied for 33 weeks, supplied approximately the same amount of protein and the same number of calories in the third to fifth weeks as in the ninth to eleventh and seventeenth to nineteenth weeks (Bransby, Bransby, Kon, Mawson and Rowland, 1950). In the last of the three periods the child was being fed five times daily from the breast, one feed of dried cow's milk having been introduced in the twelfth week (Bransby, 1950). The story is probably typical of a large number of lactations. The output of from 700 to 800 g. milk is often reached by the end of the first

1

fortnight of the baby's life and does not increase with the baby's weight. It can, therefore, be adequate only for a limited term, which depends on such highly variable factors as the growth rate and calorie requirement of the individual child; for most normal children, growing at the rate usually considered satisfactory, with the birth weight doubled about the end of the fifth month, the term is from 3 to 4 months. The Calorie value of 750 g. breast milk is about 500, of which about 9 per cent are derived from protein.

Breast milk seems to be remarkably more efficient than any other infant food and any satisfactory substitute must contain much more protein, and supply more calories. By the beginning of the second year, the protein requirements of the normal child, now on a mixed diet, will have increased four- or five-fold, although the birth weight has only been trebled. A child 12 months old, eating a good diet of the conventional kind shown on p. 11, but taking only 1,000 Calories, would have 45 g. of protein, of which about 70 per cent would be from animal sources. The average protein intakes found by Widdowson (1947) for British children in the second year of life were slightly lower, about 40 g. daily, with the same percentage derived from animal protein. A specimen diet (Paterson and Smith, 1939), set out in Table 1, has 18 per cent of its calories in the form of protein, but the diets of Widdowson's children had only from 12 to 13 per cent.

TABLE 1

Composition of children's diets at ages up to 30 months: comparison between the composition of human milk and of diets recommended by Paterson and Smith (1939) and recorded by Widdowson (1947)

Nature of diet	Age of child (months)	No. of Calories	Protein (g./day approx.)	Percentage of calories from:			Percentage of protein from:			Ca	P
				protein	fat	carbo-hydrate	animal sources	milk	cereals	(g./day)	
Breast milk ..	3–4	500	11	9	47	44	100	100	0	0·25	0·11
Mixed:											
Paterson and Smith ..	18	1,350	60	18	33	49	73	41	22	1·10	1·20
Widdowson		1,150	40	13	38	49	70	47	16	0·80	0·83
Mixed:											
Paterson and Smith ..	30	1,570	60	15	34	51	62	30	30	0·95	0·75
Widdowson		1,400	45	12	38	50	65	34	20	1·10	0·90

The authors of the specimen diet gave details also of mixed diets suitable for children 2½ years old. Their diets supplied an average of 60 g. protein daily, of which 62 per cent was of animal origin. Widdowson's children of between 2 and 3 years old had only 45 g. protein daily, 65 per cent of it also was of animal origin. Paterson and Smith's mixed diets had 15 per cent of the calories as protein, and Widdowson's only 12. Some of the data are summarized in Table 1. The figures from the two sources agree fairly well and a compromise between them represents roughly the requirements of children in the first years of life. The validity of the assumption that intakes may be a guide to requirements has been discussed by Widdowson (1947).

The Table makes clear the magnitude of the task involved in attempting to replace the animal protein in children's diets by protein of plant origin. On a

good mixed diet containing fair quantities of cow's milk, the animal protein usually forms about two thirds of the total, and it is nearly always in association with considerable amounts of fat. The omission of the animal protein will therefore involve, directly or indirectly, nearly half the total calories.

The Composition of Breast Milk

Breast milk, although it may be ideal for only a limited period, represents the highly successful development of a food for children. The account which follows concentrates on what may be the ingredients of its success.

AMINO-ACIDS

The amino-acid composition of human milk has been the subject of several investigations, and two of the more recent sets of results are given in Table 2. They are for mature milk containing 1·5 per cent of protein. The percentage in colostrum is almost twice as great, but there is a rapid fall in the first few days

TABLE 2

Amino-acids in mature human milk according to Williamson (1944) and Block and Mitchell (1946–7)

Amino-acid	Amino-acid content according to:	
	Williamson* (mg./100 g.)	Block and Mitchell† (mg./100 g.)
Arginine	67	64
Histidine	25	42
Lysine	94	108
Tyrosine	73	78
Tryptophan	31	28
Phenylalanine	77	84
Cystine	41	51
Methionine	29	33
Threonine	63	69
Leucine	228	147
Isoleucine	75	112
Valine	66	132
Alanine	35	
Glycine	0	
Proline	80	
Glutamic acid	230	
Aspartic acid	116	
Serine	69	

* The values relate to milk having 1·5 per cent protein.
† The values shown are calculated from Block and Mitchell's figures, which are given for 16·0 g. nitrogen, on the basis of 1·5 per cent protein in breast milk.

of lactation and a slower fall later. The percentage in mature milk may fall to 1·0 or even lower. It has not been discovered why colostrum should be so rich in protein. It may be a fortuitous result of the fact that the first milk contains much cell-debris from the tissues of the newly awakened mammary gland, but

it may have some fundamental relation to the infant's early needs. Block and Bolling (1946) analysed the protein in the pooled milk of six young mothers in the second to ninth days after parturition, and found more arginine and cystine, but less methionine, leucine, isoleucine and valine, than in the protein of mature milk. No conclusions could be drawn from the differences. It has been suggested from analogy with the first milk of other animals, especially the cow and sheep, that human colostrum may contain antibodies and other substances of particular benefit to the newborn child, but the evidence for the human species is not good. Tested on rats, human colostrum seemed to be a more perfect food than the mature milk when the amount of protein supplied was the same, and it was suggested that the presence of an "animal-protein factor" might have been responsible (Scott and Norris, 1949).

Only one comment will be made at the present stage on the data in Table 2. Comparison with other values given by Block and Mitchell (1946–7) shows that very few proteins have as large an amount of cystine or tryptophan as human milk, most of them having only one half to one third as much (see Table 12, p. 46).

CARBOHYDRATE

The carbohydrate of breast milk is almost entirely lactose. Minute traces of glucose and other sugars may be present also but are probably of little importance (Polonovski and Lespagnol, 1931). It is difficult to see why the disaccharide, lactose, and not a monosaccharide should be the sugar of " choice " in milk. The hydrolysis of lactose *in vitro* cannot be effected by weak acids, such as citric acid, which easily split sucrose; mineral acids are needed (Davies, 1939). The products of hydrolysis are glucose and galactose, and the galactose is apparently converted almost simultaneously into glucose, either in the intestine or after absorption in the blood (McCollum, Orent-Keiles and Day, 1939). It was previously held that there might be an advantage to the child if the conversion of the aldose involved a delay; the fact that aldoses cannot be fermented was probably the basis of the idea. It is now known, however, that the blood sugar of a child receiving breast milk rises almost as promptly as if glucose were being given (Smith, 1945), so that hydrolysis must proceed very rapidly, but some lactose may reach the large intestine where it is utilized by *Lactobacillus acidophilus* and possibly by other bacteria of importance in nutrition (Platt and Moncrieff, 1947–8). Even before the possibility of bacterial synthesis of vitamins was considered, the value of lactose for the production of an acidic medium in the gut was recognized. Measures for the artificial achievement of this end, such as the introduction of acidophilus bacilli into the diets of children, have been successfully adopted for many years. Other carbohydrates probably have less effect on the intestinal flora (Hudson and Parr, 1924).

The alteration of the hydrogen ion concentration in the intestine brought about by the presence of lactose, or by some other specific property of milk, has been shown to favour the absorption of minerals, especially calcium and phosphorus (Robinson and Duncan, 1931). Their absorption is not especially favoured by other sugars (Bergeim, 1926).

Galactose may be of special value to the infant as an ingredient for the rapid synthesis of glyco- and galactolipids, which are probably produced in large quantities in the first few weeks of life (Mathews, 1939). Galactose is found in the medullary sheath of nerve, and if the infant cannot synthesize enough the provision of this in the diet may be of importance.

The production of lactose is probably the unique prerogative of the mammalia; reports of its isolation from one or two fruits seem to be regarded with some scepticism. The amount found in human milk is from 6 to 7 per cent, which is much higher than the amount in the milk of other species. There was in former years a considerable body of clinical opinion inclined to the view that lactose in large quantities could not be tolerated by children. Gerstley (1930) seems to have disposed of the fear by pointing out that the addition of extra lactose to the diets of children did not of itself cause gastro-intestinal upsets. His clinical experience supported that of Barenberg and Abramson (1930), who gave large amounts, sufficient to supply up to 15 g. per kg. body weight, to infants with effects that seem to have been entirely beneficial.

FAT

The amount of fat needed by the infant, and the form in which it should be supplied, are uncertain. Estimates of the amount of fat in human milk vary between 3·0 and 4·5 per cent and, in the extensive analysis given by Davies (1939) of the milk of various mammals, few of the values for fat are so low. The adult man can certainly keep healthy on a diet containing very little fat (Brown, Hansen, Burr and McQuarrie, 1938). He can synthesize fats from other ingredients in the diet (Longenecker, 1943), and the foetus can almost certainly do the same (Smith, 1945). Premature infants may gain weight better if the fat in their diet is restricted (Stevenson, 1947), and it is certainly easy to produce gastro-intestinal upsets in all young children by giving them excessive amounts of fat.

The fat of human milk contains considerable quantities of linoleic, lauric and myristic acids. Their presence, and the absence of butyric acid and other saturated acids of low molecular weight, make human-milk fat more analogous to a vegetable fat than to other fats of animal origin (Hilditch and Meara, 1944).

It is possible that human infants may need a small quantity of preformed fat or of unsaturated fatty acids. If they are given diets which are almost fat-free, the serum fatty acids have a low iodine number, and eczema and other skin lesions may develop (Holt, Tidwell, Kirk, Cross and Neale, 1935; Brown, Hansen, Burr and McQuarrie, 1938). Rats on fat-deficient diets have similar changes in their blood, and develop a scaly condition of the skin which is cured when small amounts of unsaturated fatty acids, particularly linoleic acid, are given (Burr and Burr, 1929, 1930; Hansen and Burr, 1932–3). Hansen (1933–4) and Faber and Roberts (1935) found that the fatty acids of the serum of children suffering from eczema had a low iodine number which rose when the clinical condition improved. There is some evidence, therefore, that in the child the maintenance of the normal level of the blood lipids may depend on the dietary supply of fats or fatty acids, and that in eczema there may be a defect in the utilization or possibly in the synthesis of fat.

Fats are obviously valuable as vehicles for the transport of the fat-soluble vitamins and as a highly concentrated form of energy. In the rat the retention of nitrogen is increased, and the amount of energy required for the metabolism of food is lessened, as the ratio of fat to carbohydrate in the diet is increased (Forbes, Swift, Elliott and James, 1946; Forbes, Swift, James, Bratzler and Black, 1946; Forbes, Swift, Thacker, Smith and French, 1946). For the same species "fat apparently conveys efficiency of utilization of food energy" (Elvehjem and Krehl, 1947), and weight gains, capacity for exhausting work, and other functions are improved by increasing the percentage of fat in the

diet (Deuel, Meserve, Straub, Hendrick and Scheer, 1947). These effects are seen most clearly when a certain minimum percentage of fat in the diet is exceeded; they are not enhanced appreciably when the percentage is raised from 10 to 30, and the necessary minimum for the child may be lower than it is for the rat.

Boutwell, Geyer, Elvehjem and Hart (1943) have suggested that the combination of milk fat and lactose may encourage the development of an intestinal flora which helps in providing the essential fatty acids, and Geyer, Boutwell, Elvehjem and Hart (1946) believe that the fat may influence favourably the utilization of galactose in synthetic processes within the tissues.

VITAMINS AND GROWTH FACTORS

The vitamin content of human milk depends to some extent on the diet of the mother and the stage of lactation. Data quoted by Clements (1949) for the vitamins in human and cow's milk are given in Table 3. A more extensive summary of knowledge concerning human milk has been made by Macy (1949). A well founded set of values is that of Kon and Mawson (1950); 750 g. of mature milk from Reading mothers in the fourth to fifth month of lactation in 1941–5 provided about 1,100 I.U. vitamin A, from 3 to 10 I.U. vitamin D, 126 μg. vitamin B_1, 190 μg. riboflavin, and 27 mg. vitamin C.

TABLE 3

Vitamin content of human and cow's milk (Clements, 1949)

Vitamin	Unit	Vitamin content of:	
		human milk (per 100 ml.)	cow's milk (per 100 ml.)
Vitamin B_1	μg.	9–14	35–40
Riboflavin	μg.	28–62	150 (approx.)
Nicotinic acid	μg.	66–330	80–90
Calcium pantothenate ..	μg.	86–584	—
Biotin	μg.	0·04–4·2	—
Vitamin A and carotene ..	I.U.	160–670	75–220
Vitamin D	I.U.	2–18	0·5–20
Vitamin E (total tocopherols) ..	mg.	0·94	<0·1
Vitamin C	mg.	3–6	2–2·5

In recent years the existence has been claimed of various substances which do not possess the properties of any of the recognized vitamins, but affect in a remarkable way the growth of certain animals. They are usually known as "growth factors", and are referred to again on p. 22. So far, there is no direct evidence that any such substances are present in human milk, but an experiment described by Albanese, Holt, Irby, Snyderman and Lein (1947a) suggested that one acid-labile substance, found in the casein of cow's milk, might be needed by the human child. If that is so, a search for the substance should be made in human milk, preferably by the method of feeding children on suitable hydrolysates of the milk itself.

INORGANIC CONSTITUENTS

"The inorganic ingredients of breast milk are as important as any of the others" (Mottram and Graham, 1948). The mineral composition of mature milk is shown in Table 4.

TABLE 4

Comparison of the amounts of proximate principles and minerals in mature human milk and cow's milk

Constituent	Unit per 100 ml.	Amount of constituent in:			Authority
		human milk	cow's milk		
			whole	diluted with equal vol. of water	
Water ..	g.	87–88	87–88		Mottram and Graham (1948)
Protein ..	g.	1·5	3·5	1·7	*ibid.*
		1·06			Macy (1949)
Carbohydrate	g.	6·5	4·75	2·4	Mottram and Graham (1948)
		7·1			Macy (1949)
Fat	g.	3·5	3·75	1·9	Mottram and Graham (1948)
		4·54			Macy (1949)
Calories ..		63	66	33	Cox and Mueller (1937)
		74·7			Macy (1949)
Calcium ..	mg.	34	122	61	Cox and Mueller (1937)
Phosphorus ..	mg.	15	90	45	*ibid.*
Iron	mg.	0·2	0·07	0·03	*ibid.*
Copper ..	mg.	0·05	0·06	0·03	*ibid.*
			0·02		McCance and Widdowson (1946)
Magnesium ..	mg.	5	13	6	Cox and Mueller (1937)
Chloride ..	mg.	36	116	58	*ibid.*
Sulphur ..	mg.	4	31	15	Shohl (1939)
		14			Macy (1949)
Sodium ..	mg.	11	61	31	Cox and Mueller (1937)
Potassium ..	mg.	48	154	77	*ibid.*
Total solids ..	g.	12·45	12·42		*ibid.*
Total ash ..	mg.	200	750		*ibid.*
Ca/P ratio ..		2·3:1	1·3:1		*ibid.*
pH		7	6·7		*ibid.*
Iodine number of fats ..		56	32		*ibid.*

The calcium of human milk is exceptionally well utilized. If it were not, the development of rickets in breast-fed children would, as Stearns (1939) has pointed out, be a frequent occurrence. Such children receive from the milk about 200 mg. daily in the first weeks of life and a little less towards the end of lactation because the concentration in the milk falls (Clements, 1949); the minimum faecal excretion is about 150 mg., and the balance retained must be close to the minimum needs. Certainly calcium from any other source must be supplied in much greater amounts if normal growth is to be supported (Jeans, 1942).

The phosphorus also of breast milk is lower than might perhaps be expected in an ideal food, but a high proportion is retained. Its retention, like that of

calcium, is determined not merely by the amount of it in the milk but also by the amount of vitamin D available.

It is often alleged that iron is another element of which the milk seems to hold too little. A calculation of the amount of iron in the bodies of newborn infants and others a few months old shows, however, that the quantities obtainable from breast milk are probably enough for ordinary growth (McCance and Widdowson, 1951a) if the normal reserve has been acquired before birth.

SOME GENERAL CONSIDERATIONS

The purpose of thus examining the composition of human milk was to establish, as far as possible, the theoretical composition of an ideal substitute. The matter is complicated because it is impossible to say exactly to what extent human milk is itself ideal; the retention of various elements from diets other than breast milk has been shown to be greater than the retention from breast milk (Stearns, 1939), but even a superior percentage of nitrogen in the body does not of itself constitute evidence of superior body-build, and, as Smith (1945) has said about minerals, there is doubt "as to where a line should be drawn above which mineral retention is not merely an experimental *tour de force*". The infant is certainly possessed of the ability to grow normally on diets of widely different composition provided that certain basic requirements are met. The composition of breast milk might enable us to define these requirements with some exactness in terms of other foods if it were not for the undoubted fact that its ingredients, or their peculiar combinations, possess special qualities. The most effective provision of adequate substitutes for those ingredients, although suggested by chemical analyses, can at present be determined only by empirical methods.

A few generalizations are perhaps permissible. The collection of amino-acids in a substitute for human milk should probably be rich in cystine or methionine, in tryptophan and in lysine. The carbohydrate should favour an acidic reaction in the gut; steps should in any case be taken to ensure such a reaction there. The fat, which seems an unimportant constituent except for its caloric value, should include a small quantity of unsaturated fatty acids. There should be ample minerals, with a generous margin to allow for imperfect absorption. Vitamins also must be provided and possibly some source of growth factor.

If the substitute is intended for the very young, the supply of galactose, and possibly of antibodies, should be considered too.

The Amino-acid Requirements of Children

CHILDREN IN THE FIRST YEAR OF LIFE

It has been found that lysine, tryptophan, phenylalanine, methionine, threonine, leucine, isoleucine and valine are amino-acids which the body of adult man is probably unable to synthesize at least in sufficient amount for his requirement (Rose, Haines and Johnson, 1942; Rose, Haines, Johnson and Warner, 1943; Rose, 1949). Rose (1949) comments on the surprising omission of histidine from the list, but has confirmed his results. It is not known whether the list is valid also for children; for them arginine, which is needed by the growing rat and dog, but not by the adults of these species, should probably be added.

A useful summary of the available information about the amino-acid needs of small children was made by Albanese (1947). The data he was able to quote were very incomplete. Their interpretation involves many difficulties, which

include the uncertainty of the correct allotment of the dietary nitrogen between growth and maintenance, and the assessment of the value of nitrogen retentions, as shown by balance experiments, without any knowledge of the optimum level. The retentions are, in addition, subject to large day-to-day fluctuations for which no cause can be found.

The relation between nitrogen retention and body weight has been studied by Czerny and Keller (1925); according to their data, a normal child aged from 4 to 5 months, weighing 5 kg., and receiving breast milk as the only food, may retain about 500 mg. nitrogen daily from a total intake of 1,750 mg. Albanese (1947) recommended a slightly higher intake of 2,000 mg. for a child of 5 kg., but, as he pointed out, Beach, Bernstein and Macy (1941) obtained excellent growth in such children with intakes of from 1,000 to 1,200 mg. The amount of 1,750 mg. would be provided, with a small margin of safety, by 750 g. breast milk containing 1·5 g. protein per 100 g.; the quantities of some of the amino-acids supplied by that amount of milk are shown in Table 5. They have been calculated from the data of Block and Mitchell (1946–7). At the present time, they are probably the best available indication of the normal child's requirements.

TABLE 5

Approximate daily intake of amino-acids by a child of 5 kg. fed on breast milk or cow's milk (Block and Mitchell, 1946–7*)

	Amino-acid intake from:	
Amino-acid	human milk, 750 g. daily (mg.)	cow's milk, 500 g. daily (mg.)
Arginine	480	740
Histidine	320	450
Lysine	810	1,290
Tyrosine	590	910
Tryptophan	210	270
Phenylalanine	630	980
Cystine	380	170
Methionine	250	580
Threonine	520	770
Leucine	1,100	1,940
Isoleucine	850	1,460
Valine	990	1,440

* The values are calculated from the data for a protein content in human milk of 1·5, and in cow's milk of 3·5, g. per 100 g. The total respective protein intakes would be 11·2 and 17·5 g. daily.

For a child fed on cow's milk instead of human milk, the total amount of nitrogen needed to secure retentions considered adequate is greater by about 50 per cent, as is shown in three sets of results collected from the literature by Albanese (1947). The amount of cow's milk, containing 3·5 g. protein per 100 g., appropriate for the 5·0 kg. child is about 500 g., and the amounts of amino-acids it contains are shown in Table 5. Compared with 750 g. breast milk, 500 g. cow's milk have considerably more of nearly all the amino-acids. The margin is smallest for tryptophan, and the largest differences are in the sulphur-containing amino-acids. The ratio of cystine to methionine in human milk is about 1·5:1

whereas it is 1:3·5 in cow's milk. The results of various experiments with rats, with adult man and with children suggest that methionine can deputize for cystine, but that cystine cannot take the place of methionine except perhaps to a small extent (Womack and Rose, 1941; Albanese, Holt, Brumback, Frankston and Irby, 1944; Albanese, Holt, Davis, Snyderman, Lein and Smetak, 1949; Best and Lucas, 1950). The largeness of the amount of cystine in human milk does, however, tempt one to the speculation that the infant may in fact utilize cystine in some special way. Tryptophan may be of importance to the child as a source of nicotinic acid (Holman and de Lange, 1950).

Shohl, Butler, Blackfan and MacLachlan (1939) found that on a synthetic diet with an enzymic hydrolysate of casein as source of nitrogen, retention was satisfactory in infants aged from 2 to 7 months, if the amount of nitrogen given was 520 mg. per kg. daily. The amounts of breast milk and cow's milk shown in Table 5 would provide 350 and 550 mg. per kg.

The method of inferring amino-acid requirements from balance studies or intakes has obvious disadvantages, and Albanese and his co-workers have tried to approach the problem more directly. They gave children aged from 4 to 12 months diets known to be deficient in a particular amino-acid and then increased the amount of it to the point at which physiological levels of nitrogen retention, and normal rates of growth, were regained. It was thus decided that the children required, per kg. body weight daily, 30 mg. L-tryptophan (Albanese, Holt, Irby, Snyderman and Lein, 1947b), 90 mg. L-isoleucine (Albanese, Holt, Davis, Snyderman, Lein and Smetak, 1948), 85 mg. L-methionine and 15 mg. L-cystine (Albanese, Holt et al., 1949). The chief source of dietary protein in the experiments was an acid hydrolysate of casein or beef protein, with cystine and tryptophan added where necessary; small amounts were provided also by brewer's yeast, introduced primarily as a source of B vitamins. The amino-acid under investigation was added in the pure L-form. There were thus always two or three sources of the amino-acid in each trial, and none of them was intact milk protein. It is now known that substances which may be needed for the growth of children are absent from acid hydrolysates (see p.23), and a further objection is that the method of depletion involves a factor for which it is difficult to make proper allowance; the length of the period of depletion determines the amount of acid needed for repletion. Some or any one of these reasons may explain the discrepancy between the figures given in Table 5 for the tryptophan, isoleucine, methionine and cystine in 750 g. breast milk (210, 850, 250 and 380 mg., respectively) and those for a 5 kg. child's requirements calculated from the figures of Albanese and his co-workers (150, 450, 425 and 75 mg., respectively).

In an attempt to meet some of the objections another method has been adopted (Albanese, Higgons, Vestal and Stephanson, 1950). The method depends on finding the "saturation point" of a test amino-acid added in increasing amounts in the pure form to the diets of children maintained in normal nitrogen equilibrium by natural foods. It was thus found that a child weighing 5 kg. would need about 1,000 mg. L-phenylalanine daily. Breast milk (Table 5) is unlikely to supply so much, and the figure may be too high.

It is possible that the form in which an amino-acid is supplied may affect the way in which it is used in the body. The concept leads to the assumption of different optimum levels for different diets; it is supported by the work of Blazsó (1938–9), who showed that, although the infant absorbed protein sulphur equally well from breast milk, cow's milk or a mixed diet, the retention was higher on the breast milk than on the other two diets. It would seem important,

therefore, in expressing requirements to refer to the sources of the amino-acids, at least until all the disturbing factors are known.

CHILDREN FROM 1 TO 2 YEARS OLD

There appears to be no satisfactory information on the nitrogen requirements of children aged from 1 to 2 years. The extreme technical difficulties make the lack easily understood, but it is very unfortunate. To obtain a rough estimate of the requirements, one of the diets recommended by Paterson and Smith (1939) for a child of that age has been analysed. The composition of the chosen diet was as follows:

On waking:	orange juice sweetened with sugar 10 g.			
Breakfast:	porridge	90 g.	whole milk	280 g.
	half an egg			
Dinner:	chicken	60 g. with mashed potatoes		60 g.
	rice pudding	60 g.	banana	30 g.
Tea:	bread	90 g.	butter	10 g.
	whole milk	420 g.	jam	10 g.

The diet provides approximately 1,350 Calories, of which 250 (18 per cent; 62 g.) are in the form of protein. Two thirds of the 250 (41 g.) are from animal sources.

The amino-acid composition of the diet has been calculated for the various ingredients from the analytical data of Block and Mitchell (1946–7). The results (Table 6) cannot be more than an approximation and they depend on a selection

TABLE 6

Approximate amino-acid composition of a specimen daily diet suitable for a child of from 1 to 2 years old (Paterson and Smith, 1939)

Amino-acid	Amount (mg.)	Percentage of total	Percentage in protein of breast milk*
Arginine	2,240	8	7
Histidine	1,100	4	4
Lysine	2,940	11	11
Tyrosine	2,270	9	8
Tryptophan	660	2	3
Phenylalanine	2,580	10	9
Cystine	620	2	5
Methionine	1,480	6	4
Threonine	2,010	7	7
Leucine	4,620	17	16
Isoleucine	3,210	12	12
Valine	3,240	12	14
Total	26,970	100	100

* Calculated from Table 5.

of ingredients which is somewhat arbitrary. The selection is, however, fairly representative, and most of the items could be replaced by others of a similar nature without greatly affecting the values. The percentage which the various amino-acids contribute to the total protein has been determined also; no

remarkable difference is revealed from the percentage of the same amino-acids in the proteins of breast milk, the figures for which are included also in Table 6. The chief contributors to the high value for arginine are the meat and cow's milk of the diet, and the milk is responsible also for the large amount of leucine.

Factors Complicating Assessment of the Value of Dietary Proteins

The assessment of the value of proteins in nutrition is a complex subject. Many factors are involved, and some which have especially to be borne in mind in planning new work will be considered here.

ANALYTICAL DIFFICULTIES AND VARIABILITY IN THE COMPOSITION OF THE RAW MATERIALS

There are technical difficulties in the analysis of proteins for their amino-acid content which make the interpretation of results uncertain (Vickery, 1945), and the difficulties tend to multiply with any increase in the number of proteins involved.

Some of the difficulties, and the degree of correlation which can be expected between the results of the analyses and of biological tests, have been discussed by Block and Mitchell (1946–7). The discrepancies, rather than the correlations, were emphasized by Jones, Caldwell and Widness (1948), and Mitchell himself (1948) expressed the opinion that though analyses are of undoubted value, feeding tests also are necessary before the complete assessment of a protein is possible.

It is further important to realize that the same plant does not necessarily have a constant amino-acid composition. It is known that there are large differences in the amounts of cystine, tryptophan and tyrosine in different varieties of soya bean (Csonka and Jones, 1934; Hamilton and Nakamura, 1940), and somewhat smaller differences in the amount of lysine (Soybean Research Council, 1949). Glycinin, the chief protein of soya, shows such variations (Csonka and Jones, 1933). The amino-acids in yeast (Block and Bolling, 1945; Von Loesecke, 1946) and wheat (Csonka, 1937; Miller, Seiffe, Shellenberger and Miller, 1950) vary with the strain, and those of rice, not only with the strain but also with the method of cultivation and the kind of fertilizer used (Kik, 1941).

Such differences may or may not have a biological importance. They might explain why it has not been possible to reproduce the results of some experiments in the supplementation of proteins. On the other hand, the growth rates were identical of five groups of rats given five kinds of soya beans, chosen because of alleged differences in concentration of their sulphur-containing amino-acids (Everson, Steenbock, Cederquist and Parsons, 1944). In this investigation large differences were discovered in the growth-promoting value of mature, immature and germinated beans, but changes in protein composition were probably not entirely responsible.

DIFFICULTIES ARISING THROUGH THE USE OF EXPERIMENTAL ANIMALS, AND THE IMPORTANCE OF SPECIES DIFFERENCES

In any growing animal, the assessment of the value of proteins is especially complicated. It is difficult to compute even the total amount of protein required, because it is utilized as a source of energy as well as for maintenance and growth (Mitchell, 1923–4a, b, 1944; Barnes, Bates and Maack, 1946). In addition, the amino-acid requirements for growth and for maintenance are not identical (Osborne and Mendel, 1919), and once the period of rapid growth has been passed, some amino-acids may be required only in very small amounts or may cease altogether to be indispensable. Thus arginine, which must be provided in the

diet of the young rat if growth is to be satisfactory (Rose, 1938), is not needed by the adult rat (Scull and Rose, 1930; Wolf and Corley, 1939; Rose, Oesterling and Womack, 1948), and the adult's requirement of histidine, leucine, phenylalanine, and lysine too may be much less (Barnes, Bates and Maack, 1946; Mitchell, 1947). The differences may depend on different rates of synthesis at the two ages, either by micro-organisms in the intestine, or by other processes in the body (Mitchell, 1948). They probably influenced results such as those of French and Mattill (1935) and Sumner (1938), who found that the biological values of various breads, and of milk and egg proteins, were considerably less for growing rats than for adults. They might explain also the results of Widdowson (1950), who with rats could detect no difference in the value for growth of the protein in bread made from flours of various extractions, provided that the breads were not given until the animals were two thirds fully grown, at a weight of about 150 g.

The growth process is one of continuous transition and its rate varies greatly from species to species. Changes in the need for protein and other nutrients at various ages are, therefore, likely to be different in different species, and analogies between a slow-growing species like man and a fast-growing species like the rat must be drawn with some caution. Nearly a hundred years ago Savory (1863) chose rats because they are "omnivorous, and will readily feed on almost any kind of diet. Moreover, from their size, they are convenient to manage." Much of the evidence for the supplementary value of proteins has been obtained with rats, which have for long held a dominant place in nutritional research. Their growth rate is so rapid that they are probably a good choice for work intended to apply essentially to the needs of children, although their need for extra protein in the growth period may be exaggerated because of that rapidity (Zucker and Zucker, 1943). They were used in establishing the concept of the indispensability of certain amino-acids which cannot be synthesized by the animal organism (Rose, 1938) and, although the direct evidence for similar needs by man has been slow to appear, that evidence has usually been confirmatory (Rose, 1949).

Study of the growth of rats on mature human milk led Scott and Norris (1949) to the conclusion that "the rat is obviously a poor experimental animal for use in attempting to evaluate a food for young infants". The evidence was three-fold: at the level of 9 per cent the protein was inadequate because it lacked sufficient of the sulphur-containing amino-acids; lactose was not tolerated; and the milk did not contain an unidentified factor present in cow's milk, yeast and liver, which is needed for rat growth. Human colostrum was slightly more satisfactory, possibly because it contained the missing factor. Henry, Kon and Mawson (1950), who used the separated, freeze-dried milk of women in early lactation, found that at the level of 8 per cent of protein its biological value in rat-feeding experiments was the same as that of separated, dried cow's milk. The human milk, however, caused diarrhoea, which was assumed to be an effect of the high proportion of lactose. Many other writers (Mitchell and Dodge, 1935; Mitchell, 1935, 1936; Yudkin and Arnold, 1934–5; Day, 1935, 1936; Ershoff and Deuel, 1944; Barki, Derse, Collins, Hart and Elvehjem, 1949) have noted the sensitivity of rats to lactose, and some have reported that they developed cataract. The ill-effects may be due to the galactose of the lactose molecule (Mitchell, 1935; Handler, 1947).

The progress of rat-feeding experiments is almost entirely judged by weight gains, and it is even necessary here to exercise some caution. It has been stated that rats can gain weight and appear to remain healthy although their livers are being damaged (Gillman, Gillman, Mandelstam and Gilbert, 1945). A few workers have analysed the bodies of the animals they had fed to ascertain whether the

expected amount of protein had been laid down (Mitchell, 1918; Scull and Rose, 1930; Carlson, Hafner and Hayward, 1946; Chick and Slack, 1948; Slack, 1948), but the method has obvious limitations and cannot always be applied. It is generally held by pig-keepers and cattle-raisers that very rapid gains in weight imply the acquisition of fat and not muscle (Mitchell, 1944), and the same undoubtedly applies to other animals, but the relative amounts of the two tissues depend also to some extent on the species (Spray and Widdowson, 1950).

In spite of the objections, the rat remains one of the most valuable of the experimental animals available for nutritional investigation. It seems reasonable to suppose that, although shades of difference in the needs of the growing rat and the growing child may at some time in the future be detected, the effects of protein supplementation are approximately the same in both species; growth will in all cases be better on the more complete mixtures. The literature relating to supplementation of the diets of the chick, pig and cow has been surveyed without the discovery of any important facts to disturb this opinion, although ruminants, with their exceptional capacity for amino-acid synthesis within the intestinal tract, may have less specific needs than non-ruminants for the amino-acids commonly accepted as essential (Miller and Morrison, 1944).

NEED FOR THE ESSENTIAL AMINO-ACIDS TO BE PRESENT
SIMULTANEOUSLY

One of the conditions for success in protein supplementation is that all the necessary amino-acids should be present simultaneously at the site where they are needed for the synthetic processes of the body.

Elman (1939) confirmed certain of his earlier experiments in which acid hydrolysates of casein failed to maintain a positive nitrogen balance in dogs unless tryptophan and methionine were added. If the tryptophan was given by injection after the rest of the amino-acids, its effect was lost. Presumably the amino-acids given first were deaminated in the liver very rapidly, before the missing acids needed for synthesis were present also. In confirming his observations, Elman found that an interval of 6 hours rendered the tryptophan useless; it had to be given simultaneously to exercise its supplementary value.

Other workers have come to the same conclusion. Henry and Kon (1946) found with rats that much of the supplementary value of Cheddar cheese for white bread, and of dried skimmed milk for potato, was lost if the foods were given on alternate days. Geiger (1948) fed rats with yeast and wheat gluten together, or alternately for 10-hour periods, and found that the first method produced excellent growth and the other none. Similar results were obtained with yeast and blood, and with other mixtures.

Melnick, Oser and Weiss (1946) stressed the importance of the rate of release of amino-acids from proteins by enzymic hydrolysis. They used soya protein, and showed that methionine was released from it at different rates according to the method which had been used for processing the raw material. All the methionine might eventually be released, but some of it might not be utilized because of delay. It would be of value to investigate the rate of release of the various amino-acids from other mixtures of proteins such as are normally found in complete diets, but this has not yet been done.

Chase and Lewis (1934) compared the rate of absorption of various amino-acids from the gastro-intestinal tract of the rat. The acids were given as their sodium salts and the rates were found to vary greatly. The absorption coefficients were as follows:

Glycine	0·84	Methionine	0·36
Alanine	0·54	Leucine	0·34
Cystine	0·44	Isoleucine	0·27
Glutamic acid	0·41	Isovaline	0·14
Valine	0·40		

If it is true that all the amino-acids are required simultaneously by the body for its process of synthesis, these rates cannot, of course, represent what happens when a complete food mixture is given.

It is not known whether the results of the animal experiments referred to above apply also to man. The subject should be investigated, because the value of mid-day school meals, and of other supplementary feeding schemes might depend on their timing in relation to the rest of the diet.

EFFECTS OF HEAT TREATMENT ON PROTEINS

A great deal of information about the effects of heat treatment on the proteins of foods was gathered together by Jacquot, Matet and Fridenson (1947). The effects have been divided, for the present purpose, into those which are harmful and those which are beneficial.

The Damage to Proteins by Heat

When peas (*Pisum sativum*) or groundnuts (peanuts) were autoclaved for an hour (Jacquot and Blaizot, 1947; Matet, Montagne and Fridenson, 1947) or when cottonseed meal was autoclaved for 2 hours (Olcott and Fontaine, 1941), the proteins appeared to decline in nutritive value. When young rats were fed on toasted wheat or rye bread or on the crust of the bread, the weight increase was not as great as when the untoasted bread or crumb was given (Morgan and King, 1925–6; Morgan, 1931; Kon and Markuze, 1931). Cooking cereals under pressure, followed by the sudden release of the pressure and the expansion of the cereal grains, was highly deleterious (Morgan, 1931; Murlin, Nasset and Marsh, 1938; Stewart, Hensley and Peters, 1943; Kuether and Myers, 1948). Autoclaving or application of dry heat damaged the total protein of dried milk (Fairbanks and Mitchell, 1935; Voegtlin and Thompson, 1936) and also the isolated milk proteins, casein and lactalbumin (Boas-Fixsen and Jackson, 1932; Chick, Boas-Fixsen, Hutchinson and Jackson, 1935).

The heating process sometimes appeared to destroy wholly or partly one amino-acid only. Thus, if heated cottonseed meal was supplemented with L-lysine, its nutritive value was partly restored (Olcott and Fontaine, 1941) and the same addition to heated casein was even more effective (Greaves and Morgan, 1933–4; Greaves, Morgan and Loveen, 1938). The observations certainly suggested that the heating had destroyed the lysine, but the matter was found not to be so simple, for Block, Jones and Gersdorff (1934) and Zittle and Eldred (1944), when analysing heated casein after acid hydrolysis, could detect no loss of lysine attributable to the heating. It was suggested that the altered nutritive value might result from the conversion of part of the protein into a form resistant to enzymic digestion in the intestine but not to acid hydrolysis *in vitro*.

Block, Cannon, Wissler, Steffee, Straube, Frazier and Woolridge (1946) made a cake from ingredients chosen for their high protein value and observed the change in the efficiency of the proteins caused by baking or other forms of cooking. The raw ingredients had a protein efficiency ratio, defined as g. growth per g. protein eaten, for rats of from 3·3 to 3·5; ordinary baking reduced the value to 2·4; drying pieces of the cake in an oven, and toasting them, caused

further large reductions in the ratio to 1·5 and 0·7, but the effect was largely counteracted by adding L-lysine to the diet. There was probably destruction of lysine and formation of enzyme-resistant linkages. Such linkages have been discussed at length by Melnick and Oser (1949); they do not seem to be produced with soya protein by even prolonged boiling, but only by excessive dry heating or autoclaving (Riesen, Clandinin, Elvehjem and Cravens, 1947; Hou, Riesen and Elvehjem, 1949).

The effects of dry heat on the amino-acids of soya beans are apparently different from those of autoclaving. Evans and Butts (1948) heated soya bean oil meal for 2 hours at 120° C. in the dry state, and found that the lysine was unchanged. As opposed to autoclaving, prolonged boiling of whole soya beans with water for even 12 hours seemed not to be harmful but to increase considerably the amount of amino-acids which could be released by subsequent enzymic treatment. It was pointed out that the boiling resembled the treatment normally used by the Chinese in preparing the bean for eating (Hou, Riesen and Elvehjem, 1949).

Lysine seems particularly liable to heat damage, but many other amino-acids are susceptible to such changes.

An explanation of the changes caused by heat may lie in the amino-sugar reaction, which was discussed in relation to nutrition by Lea and Hannan (1950). By this, amino-acids combine with reducing sugars at a rate which, in the right state of humidity and even at room temperature, is sufficient to be of importance in the storage of a food such as dried milk (Henry, Kon, Lea, Smith and White, 1946; Lea, 1948; Henry, Kon, Lea and White, 1948). The reaction has a high temperature coefficient (Lea, 1950) and it may be responsible for much of the damage caused to protein by heat. The amino-acids inactivated are those which have free carboxyl or amino-groups, or other active groups such as the imidazole of histidine, or the sulphydryl of cystine or methionine. Some of the groups may combine directly with the sugar, but the free carboxyl groups of glutamic and aspartic acids may react with lysine. The linkages produced usually resist enzyme digestion but can be broken by acid hydrolysis. Even acid hydrolysis may not be wholly effective (Evans and Butts, 1948). The amino-acids are more easily affected if they are in the free state than if they are combined in protein.

The multiple effects of the reaction have been demonstrated. Patton, Hill and Foreman (1948a, b) refluxed casein and soya globulin with glucose, and found that the lysine, arginine and tryptophan of the one, and the lysine, arginine, tryptophan and histidine of the other, were appreciably inactivated. Even "pure" casein heated by itself may lose lysine (Stokes, Gunness, Dwyer and Caswell, 1947) and histidine (Greaves and Morgan, 1933–4; Greaves, Morgan and Loveen, 1938), due possibly to the action of galactose which is always present as an impurity (Rimington, 1936). For investigating the behaviour of the amino-acids of soya globulin in the presence of sugar, Patton, Hill and Foreman (1948b) preferred the isolated protein to the naturally occurring mixture of proteins in the beans because they found that, as hydrolysis proceeded, carbonyl compounds present in the bean carbohydrates, or produced from them, reacted with the amino-groups of the released acids.

The effect of autoclaving soya beans, or meal made from them, has several times been investigated. Autoclaving the meal for 1 hour at 130° C. made 30 per cent of the lysine in the product of acid hydrolysis unavailable to *Streptococcus faecalis* R. Autoclaving for 4 hours at 120 C. impaired the ability of the meal to support the growth of chicks, but addition of lysine to the diet improved the growth rate. The improvement occurred even if the lysine was autoclaved unless

the autoclaving was done in the presence of the carbohydrate, "Cerelose", when the lysine appeared to become unavailable to the chick (Stevens and McGinnis, 1947). Evans and Butts (1948) pointed out that although soya meal does not normally contain any reducing sugars, the heating probably caused inversion of some of the sucrose which is its principle carbohydrate. They autoclaved the meal even more strongly, for 4 hours at 140° C., and found that 85 per cent of the lysine and cystine, and about half of the arginine, glutamic acid, histidine and methionine were altered to forms which resisted enzymic hydrolysis *in vitro* (Evans and Butts, 1949a, b).

The linkage between methionine and sucrose has received some special study. Chicks fed on overheated soya protein were unable to digest a certain part of it which was found to contain more than a quarter of the methionine sulphur (Evans and McGinnis, 1946; Evans, McGinnis and St. John, 1947). The suggestion was made that the excessive autoclaving caused the formation of substances which interfered specifically with the normal absorption of methionine, or with its metabolism (Evans and McGinnis, 1948).

The apparent anomaly that heat may have at the same time a beneficial and a harmful effect on the proteins in soya products is explained in the next section.

The Direct Improvement of Proteins by Heat

There are some plant proteins which are improved by heat treatment, provided that it is not too vigorous or prolonged.

McCollum, Simmonds and Pitz (1917) fed rats on the haricot bean (*Phaseolus vulgaris*) but obtained very poor growth although the percentage of protein in the diet was 19·6. They attributed part of the failure to the excessive fermentation of hemi-celluloses, but found that the addition of from 3 to 4 per cent of casein greatly improved growth, and the addition of 9 per cent restored it to normal. Osborne and Mendel (see Johns and Finks, 1920) showed that if the isolated protein, phaseolin, from the beans was cooked in water, its biological value was enhanced. The result was confirmed by Johns and Finks (1920) and by Waterman and Johns (1921) who discovered also that not merely the isolated protein, but the protein in the whole meal of the bean, was improved by boiling. Boiling increased the amount of protein which could be digested by enzymes *in vitro*, and the suggestion was made that one of the effects of heating might be the destruction of some toxic substance.

Cottonseed meal is another foodstuff known to be improved by cooking. Given raw to pigs, it causes a condition which resembles beriberi (Rommel and Vedder, 1915). Osborne and Mendel (1917a) found that it contained a toxic factor which could be extracted by ether or destroyed by heating. The factor is now known as gossypol, and resides in the kernel of the cottonseed (Jones and Waterman, 1923). The effect of heating may be to change it so that it becomes relatively insoluble, and therefore innocuous (Gallup, 1928).

Soya bean meal was another food investigated by Osborne and Mendel (1917b) and again they found that cooking greatly improved the biological value. They worked with rats, and considered that one of the benefits of cooking might be to increase palatability. Various other workers, feeding chicks, cows, pigs and sheep as well as rats and other laboratory animals, observed that cooking soya nearly always improved its nutritive value. The results were not entirely consistent, so the different methods of preparing soya bean flour were investigated; as a result Hayward, Steenbock and Bohstedt (1936a) decided that the ordinary hydraulic process, in which the maximum temperature reached was about 82° C., and the

low-temperature expeller process, in which the oil was expelled at 105° C., produced meals of low value, but that the hydraulic process, working at a higher temperature of from 130° to 150° C., was much more effective. They also tried adding large amounts of casein to raw, ground soya beans, and fed rats on the mixture with a protein level of 32 per cent. It gave good growth, showing that it was the protein in the uncooked soya material which was at fault. Subsequently, the same authors reported that the benefit of the high-temperature expeller process could be obtained also by autoclaving the raw ground soya beans for 1 hour at 15 lb. pressure, or by adding 0·3 per cent of L-cystine (Hayward, Steenbock and Bohstedt, 1936b). The addition of cystine after processing or autoclaving had no added beneficial effect, and it was suggested that the heating had made available the cystine already in the soya material. The extent of the improvement which can be brought about by suitable heating is shown in Table 7. It will be seen that even when casein was added to the raw meal, the weight gains, though improved, were still below those obtained with autoclaved meal.

TABLE 7

Growth of rats given ground soya beans treated in various ways (from Hayward, Steenbock and Bohstedt, 1936a, Table 4)

Method of treating ground soya beans	Amount of protein in diet (%)	Gain in weight per g. protein eaten (g.)
Removal of oil by ether extraction at max. temp. of 26° C. ..	18	0·31
Application of dry heat at 135°C. for 3 hr.	18	0·48
Heating in sealed bomb in autoclave at 125° C. for 1½ hr. ..	18	0·93
Autoclaving at 125° C. for 1½ hr.	18	1·22
No treatment; 18 per cent casein added	32	0·93

Johnson, Parsons and Steenbock (1939) found that the nitrogen and sulphur of soya were much better retained from meal produced at 150° C. by the high-temperature expeller process than from the raw bean; they thought that the heating made available a complex containing these two elements, but Mitchell and Beadles (1939) pointed out that even when the cystine deficiency of the soya bean had been corrected, there was still further improvement to be obtained by judicious heating. Overheating is known to be harmful (Bird and Burkhardt, 1943; Parsons, 1943). Miller and Morrison (1944) made nitrogen balance experiments on lambs and found that with toasted, solvent-extracted meal, the apparent digestibility of the protein was 71 per cent, and 26 per cent of the total nitrogen was retained, but that with raw soya the corresponding values were 63 and 18. Addition of the oil extracted from the soya beans did not result in any improvement. Contrary to expectation, the biological value of the soya protein was not greatly increased by the heat treatment, but the treatment may have been inadequate. Real light was thrown upon the nature of the benefit conferred on soya products by heating when it was discovered that the bean contains a trypsin inhibitor.

The Indirect Improvement of Proteins by Heat: Removal of the Trypsin Inhibitor

In 1944, Ham and Sandstedt described the extraction from the soya bean by dilute acid or 45 per cent ethanol of a substance which inhibited the breakdown of protein by trypsin. The inhibitory power was demonstrated *in vitro*. It was lost if the original material or the alcoholic extract was autoclaved or if the extract was dialysed. The authors at the same time referred to work carried out previously at the Nebraska Experiment Station and subsequently published, which had shown that a factor inhibiting the growth of chicks could be extracted from soya bean with acid, leaving a highly nutritious residue (Ham, Sandstedt and Mussehl, 1945). It was stated also that the inhibiting substance was apparently lost if the aqueous extracts were treated with 60 per cent ethanol. It was later pointed out, however, by Bowman (1946) that this was probably a mistake, caused by the use of kaolin for removing protein; kaolin adsorbed the inhibiting substance as well as the protein.

Bowman (1944) showed that aqueous extracts of soya beans and haricot beans (*Phaseolus vulgaris*) contained fractions which greatly hindered the tryptic digestion of casein. The proteins in the extracts were precipitated at pH 4·0, and the supernatant fluid contained nearly all the fractions active in retarding protein breakdown. Acetone precipitated the active fractions from the extracts of both kinds of bean, but much of the active fraction from soya was apparently soluble in ethanol. The result suggested that two different substances might be involved. Mirsky (1944) investigated the fibrolysin obtained from a filtrate of a broth culture of β-haemolytic streptococci and found that its activity was greatly reduced by a trypsin inhibitor which Kunitz and Northrop (1936) had isolated from pancreas, or by extracts of soya bean. Kunitz (1945) found, however, that the inhibitor from soya was precipitated when heated with a 2·5 per cent solution of trichloroacetic acid and did not diffuse through collodion or cellophane membranes, while the inhibitor from pancreas did not possess these properties. He prepared the soya inhibitor in the pure, crystalline state (Kunitz, 1946), and decided it was a protein of the globulin type, soluble in dilute acid, alkali or salts. It was slightly soluble in water in the pH range from 4·2 to 4·8. Its maximum light absorption was at 280 mμ. and the minimum at 252 mμ., which is typical for a protein. It contained 16 per cent nitrogen and less than 0·01 per cent phosphorus, and was free from carbohydrate. The yield of the pure protein was about 1 g. for each kg. of solvent-extracted soya flour. Kunitz (1947a, b) subsequently showed that the protein had a molecular weight of about 24,000 and an iso-electric point at pH 4·5. It combined with an equal weight of trypsin, but did not affect pepsin, and had only a slight inhibiting effect on chymotrypsin. It was denatured when heated in dilute acid or alkali solution at temperatures of over 40° C. The denaturation was reversed on cooling unless the heating was suitably prolonged.

Klose, Hill and Fevold (1946) separated two fractions of soya protein, one soluble and the other insoluble in acid at pH 4·2. The acid-insoluble fraction increased considerably in biological value when autoclaved at atmospheric pressure for 30 minutes, but if some unheated material was added to the heated, the value returned again to a lower level. The acid-soluble fraction, which was precipitated by 2·7M ammonium sulphate, contained a high concentration of a growth inhibitor, which, on being added to casein reduced its growth-promoting value. Bowman (1946) decided that soya contained two anti-tryptic factors, both soluble in water, but of which one was precipitated by

60 per cent ethanol while the other was soluble in it, but was precipitated by acetone. The two substances could be separated also by their different responses to treatment with ammonium sulphate and trichloroacetic acid. The fraction insoluble in acetone contained about 5 per cent phosphorus. Bowman (1948) has more recently found that there are three soya factors, not two, and that they are all capable of separation by using different concentrations of ammonium sulphate.

Extraction with $0.05N$ hydrochloric acid for 2 hours removed nearly the whole of the inhibiting material from the soya bean (Borchers, Ackerson and Sandstedt, 1947); the hydrogen ion concentration had little effect on the amount extracted, and the extraction was, therefore, best carried out at pH 4·2, the iso-electric point of the soya proteins. The inhibiting power was destroyed by autoclaving suspensions in water for 60 minutes at 5 lb. pressure, 30 minutes at 10 lb., 20 minutes at 15 lb. or 10 minutes at 20 lb., or by passing steam through the suspension for 90 minutes. Dry heat at about 135° C. for 4 hours toasted the meal without destroying the antitryptic activity. Subsequently, Borchers, Ackerson and Mussehl (1948b), on the strength of evidence obtained from chick growth experiments, recommended that the period of autoclaving should be 20 minutes at 15 lb. pressure. They pointed out that a test for the presence of inhibitor can be used to ascertain whether the heat treatment has been carried out adequately, but that such a test will not show if there has been overheating which is liable to harm the soya protein (p. 16). Westfall and Hauge (1947, 1948), who described a simple test for the antitryptic power of extracts of soya, decided that the optimum conditions for its destruction were autoclaving at 108° C. for 15 minutes. They noted that if the temperature was raised to 120°C., some deterioration occurred in the ability of the protein to support the growth of mice. Methods of test were given also by Northrop, Kunitz and Herriott (1948).

McGinnis and Menzies (1946) reported that papain digestion for 14 hours at 37° C. improved the value of soya bean flakes for chick growth as much as autoclaving them for 30 minutes at 120° C. The finding requires explanation. It seems to suggest that the enzyme might have inactivated the trypsin inhibitor, but Desikachar and De (1947) found that digesting soya bean meal with papain for 48 hours at 50° C. caused only a slight loss of the inhibitor. The results of their rat-feeding experiments certainly suggest that the inhibitor was still active after the digestion, as Klose, Greaves and Fevold (1948) pointed out.

The amino-acid composition of the crystalline inhibitor and of trypsin was examined by Work (1948) who used paper chromatography after hydrolysis with hydrochloric acid. The inhibitor and trypsin both contained aspartic acid, glutamic acid, glycine, alanine, serine, threonine, valine, leucine, isoleucine, histidine, proline, tyrosine, arginine, lysine and cystine. They contained also phenylalanine and methionine, but the amounts in trypsin were very small.

In an interesting observation of what is presumably an effect of the trypsin inhibitor in soya, it was found that the pancreas of chicks fed on the raw meal as the only source of protein became enlarged and its proteolytic activity was increased (Chernick, Lepkowsky and Chaikoff, 1948). The liver was not affected. The abnormalities were not prevented by adding methionine to the diet although growth was improved. The work should be repeated on other species in whose nutrition the inhibitor has been found to be of importance.

Raw soya bean has been shown to produce some other remarkable effects. Its presence in the diet of rabbits and chicks leads to a rise in the uric acid and

urea content of the blood; in the rabbit the blood lipase and cholesterol also may rise, and necroses may occur in the kidney fat (Horvath and Chang, 1925; Horvath, 1926, 1930; Tso and Ling, 1930–1). In the rat a necrotic condition of the liver may be produced (Matet, Matet and Fridenson, 1945). Some of these changes may depend on the metabolism of the sulphur-containing amino-acids (Matet, Matet and Fridenson, 1949), on which the trypsin inhibitor possibly has a particular influence. The changes should certainly be re-investigated to see if they depend on the presence of the inhibitor. It may be mentioned that haemorrhages, and a rise in blood urea, were found by Zucker and Zucker (1948) in rats given a diet which, as it now appears, was probably deficient in vitamin B_{12}.

Substances inhibiting tryptic activity have been found by Borchers and Ackerson (1947) in the peanut or groundnut (*Arachis hypogaea*), chick pea (*Cicer arietinum*), black-eyed pea (*Vigna sinensis*), mung bean (*Phaseolus aureus*), scarlet runner (*Phaseolus coccineus*), lima bean (*Phaseolus lunatus*), velvet bean (*Mucuna deeringiana*) and carob bean (*Ceratonia siliqua*), but not in lentils (*Lens esculenta*), garden peas (*Pisum sativum*), oats, barley, rye, wheat, maize, flax (*Linum usitatissimum*) or millet (*Sorghum vulgare*). The identity of some of these substances with the soya inhibitor has been suggested (Klose, Hill, Greaves and Fevold, 1949; Bowman, 1945).

The discovery of the inhibitors has rendered obsolete much of the work by which it was sought to explain the beneficial action of heat on soya, but the observations made on the harmful effects of overheating retain their value. It must be obvious that unless the heating conditions have been exactly defined, accounts of experiments which have involved feeding with soya beans cannot always be allowed the value which has previously been accorded to them, and it is unfortunately true that very few accounts are satisfactory in this respect. The present state of knowledge concerning the advantages and disadvantages of heat treatment does not, however, justify the complete disregard of all the older work on soya. If the reports of rat experiments (Table 7) and child-feeding trials (Table 9, p. 28) are examined, it will be found that a considerable degree of success was achieved in many instances, although it seems unlikely that the inhibitor had been destroyed. It cannot be claimed that there is yet full understanding of the effects of the trypsin inhibitor or of overheating on nutritive value. Borchers, Ackerson and Mussehl (1948a) decided that, although the various inhibitors all entered into combination with trypsin, they did not all affect growth equally, and Simon and Melnick (1950) brought forward evidence that the power to inhibit tryptic activity and the power to inhibit growth might be affected differently by heat. When aqueous suspensions of soya bean were heated, they retained the power to inhibit the action of trypsin *in vitro*, but produced better growth in rats than the raw soya. It was already known (Kunitz, 1947a) that the trypsin inhibitor when denatured could be digested by pepsin, and Simon and Melnick pointed out that if the inhibitor had been reduced by mild heating to a condition of "incipient denaturation", peptic digestion *in vitro* might destroy it completely. They found also that overheating of soya protein, though it might lower the protein efficiency, as expressed by g. increase in weight per g. of protein eaten, could yet enhance the digestibility of it by trypsin *in vitro*.

Other writers have suggested that the action of the inhibitor may be less simple than has been supposed. Westfall, Bosshardt and Barnes (1948) referred to possible "indirect mechanisms whereby an inhibitor of proteolytic activity

could exert a deleterious effect in the intestinal tract or in the animal body aside from the inhibition of tryptic digestion of dietary protein within the intestinal tract", and Borchers, Ham, Sandstedt, Ackerson, Thayer and Mussehl (1947), who found that the inhibitor did not affect gross digestibility, pointed out that its action might be to prevent the complete utilization of part of the soya protein after absorption. Lewis and Taylor (1947) made a similar suggestion (see below).

In whatever way the trypsin inhibitor works, the simple practical point does seem clear that it can be effectively destroyed in soya products by autoclaving for from 15 to 20 minutes at 15 lb. pressure. The temperature of 120° C. should not be exceeded because the soya may be damaged.

THE TRYPSIN INHIBITOR IN HUMAN NUTRITION

Very little is known about the effect of the trypsin inhibitor in human nutrition but some inferences may be drawn from such experiments as those of Cahill, Schroeder and Smith (1944). Adult subjects were given diets containing whole soya beans and soya bean flour, both of which had been autoclaved for an hour at 15 lb. pressure. The treatment probably destroyed the inhibitor, since the biological value of the soya protein was found to be about 92 to 93 on both diets, the biological value of egg protein being taken as 100. The figure is considerably higher than that often reported in the results of experiments with soya feeding. For instance, Chang, Li and Lan (1941) found that the protein of soya curd had a biological value for adult man of only 64, while that of a mixture of soya and egg protein was 77.

Lewis and Taylor (1947) made a direct trial of the importance of the inhibitor by giving two men diets which provided 75 g. of soya protein as soya flour which was raw or had been autoclaved for 1 hour at 15 lb. pressure. The nitrogen retention was about 20 per cent greater when the flour was autoclaved, but with the raw flour the stool nitrogen was not increased. The latter observation, which implies that the digestion of the soya protein and its absorption were the same on both diets, needs confirmation.

EFFECT OF OTHER INHIBITORS IN PLANTS

An oil which contains a substance inhibiting the digestion of starch *in vitro* by pancreatic amylase can be obtained by extracting haricot beans and soya beans with ether (Bowman, 1943). The action of the substance *in vivo* should not be neglected in protein studies because it might prevent carbohydrate digestion, and the resulting diarrhoea might hinder the free utilization of dietary proteins.

DISTURBING EFFECT OF UNRECOGNIZED GROWTH FACTORS

In planning experiments to show the value of any dietary component, the practice has always been to supply diets which satisfy all the other known requirements of the animal. It is obvious that if unknown factors affecting growth are lacking in an experiment where growth is the criterion, the results will not be reliable. As more and more of the vitamins and allied substances were recognized and produced in the pure form, it became clear that there were still other factors needed for the satisfactory growth of animals. A large literature has grown up on the subject. No attempt will be made to survey it here, and it will be discussed only as far as appears relevant in studying the effects of feeding children on diets predominantly of plant origin.

The unknown factors were originally thought to occur almost exclusively in connexion with animal protein. Liver was recognized at an early stage as a source of the so-called "animal-protein factor", but Cary and Hartman (1947) found their Nutrient X in cow's milk, cheese, beef and pork muscle as well as in liver. It was also in some plants, alfalfa, lettuce, timothy grass and Kentucky blue grass, but not in others, wheat, maize, soya bean, linseed, carrot and tomato, or in yeast. Rats fed on diets from which Nutrient X was excluded failed to grow well and had enlarged kidneys; increase in the percentage of protein depressed growth further instead of enhancing it.

It was subsequently decided that at least part of Nutrient X was the substance named vitamin B_{12} (Hartman, Dryden and Cary, 1949), which appears to be needed as a growth factor not by the rat only, but by other species such as the young chick (Carlson, Miller, Peeler, Norris and Heuser, 1949; Wiese, Petersen and Lampman, 1949) and the weanling pig (Luecke, McMillen, Thorp and Boniece, 1949). It may be that it is of fundamental importance in the utilization of protein, and that its presence may reduce the need for methionine and other possible donors of methyl groups; transmethylation may perhaps be more effective in the presence of vitamin B_{12}, or a partial deficiency of it may create or stimulate metabolic processes which require an excess of methyl groups (Gillis and Norris, 1949a, b; Cunha, Hopper, Burnside, Pearson, Glasscock and Shealy, 1949). The requirement, in confirmation of one of Cary and Hartman's original observations, increases with the proportion of protein in the diet.

It now seems that vitamin B_{12} occurs rarely, if at all, in plants, and the vegetable sources mentioned by Cary and Hartman may have provided not vitamin B_{12} but some other necessary material (Zucker and Zucker, 1950).

Vitamin B_{12} may be needed also by the growing child. Eleven children who were growing poorly, some because they were malnourished and some from "simple growth failure", were given 10 μg. vitamin B_{12} by mouth daily (Wetzel, Fargo, Smith and Helikson, 1949). Five of them responded to the treatment by greatly accelerated growth; they improved also in physical vigour, in alertness and, most markedly, in appetite. The most dramatic result was seen in one child who had severe allergic bronchitis; his asthmatic attacks ceased in the first week of therapy, and the possible significance of the success is discussed in relation to the effect of vitamin B_{12} on protein metabolism.

The experiment of Albanese, Holt, Irby, Snyderman and Lein (1947a) already referred to (p. 6) consisted in feeding three normal infants of from 5 to 11 months old on an acid digest of cow's milk casein, fortified with L-tryptophan and L-cystine, and on enzymic digests of casein or lactalbumin. The acid digest was much less successful in supporting growth and promoting nitrogen retention and it seemed reasonable to conclude that casein contained a substance, destroyed by acid, which was required by children for growth. An acid-labile substance needed by growing mice was already known. It was the strepogenin of Woolley (1945, 1946), but it was not possible to establish whether or not it was the substance lacking from the acid digest.

In the experiments with vitamin B_{12} pure crystalline material was used, but the usual source is a concentrate made from liver or from cultures of micro-organisms; some of the micro-organisms are present in cow manure. Such concentrates have been found to show actions additional to those of pure vitamin B_{12} (Cunha, Burnside, Buschman, Glasscock, Pearson and Shealy, 1949). On the other hand, animal-protein factor, produced by a non-motile rod-shaped organism from hen faeces, behaved like vitamin B_{12} when added to

chick diets, but when fishmeal was added too there was further improvement in growth (Wiese, Petersen and Lampman, 1949). At the present time it seems advisable to admit the possible existence of a number of growth factors, and to await the identification of those which are of importance in human nutrition. Meanwhile their possibly disturbing influence should not be forgotten in nutritional studies, particularly where growth is the criterion.

The Need for Milk Substitutes

An adequate substitute for breast milk is needed whenever a mother is unable or unwilling to satisfy her child. The substitute would be ideal if it were suitable for use at all ages and not only in the first few months of life. When it had fulfilled its duty of replacing the breast milk, it could then continue to serve as an effective supplement to the rest of the diet.

The need of a substitute for cow's milk arises most obviously and frequently in countries where dairy animals are scarce or even unknown, in parts of India for instance, and in most of China, but there are other reasons which have made the substitutes necessary. Thus Hindes (1926) writing of his experience in Georgia, Armenia and Transcaucasia said that in those countries, in summer, children who were not given milk had much less than the usual amount of illness. He found that the children's tolerance of cow's milk declined as the temperature rose, which he attributed to reduction in amount and bactericidal power of the digestive juices in hot weather. The cow's milk available was un- doubtedly grossly contaminated in summer, and it is not surprising that Hindes found no evidence that the unfortunate children who drank it showed any greater resistance to disease than those not having milk. Gomez, Ramos, Bienvenu and Cravioto (1950) similarly reported that in Mexico the quality of the ordinary milk is so bad that paediatricians try to prevent its being given to children.

Among children in many parts of the world where there is not a good supply of milk, a disease occurs which seems to be largely the result of protein deficiency. Williams (1933) who first recognized the disease as a clinical entity called it by its native name, *kwashiorkor*. The literature has been reviewed by Waterlow (1948), Brock and Autret (1952) and Davies (1952). Milk has usually been found to be curative, and was found to be so by the present writer also (Trowell and Dean, 1952) while working in Uganda where lack of protein in the diet seemed almost certainly to be the cause of the disease.

In countries where the supply of cow's milk has been plentiful, and the quality good, the need for a substitute has arisen because of the so-called sensitivity to cow's milk some children are believed to develop. The present-day commercial production of milk substitutes is designed almost entirely to fill this need. The chief manifestation of intolerance is eczema, and most clinicians are convinced of the close connexion between the skin lesions and the presence of milk in the diet. In the acute stage of eczema and of other illnesses, the iodine number of the serum lipids is lowered (Stoesser, 1936). The addition of soya bean oil, which itself has a high iodine number, to the diet during the acute stage of eczema may restore the iodine number of the blood fats to the normal level, with improvement in the clinical condition (Stoesser, 1947). The observation might explain the successes often attributed to soya preparations when used instead of cow's milk for treating eczema; the allergen is removed, and a therapeutic agent is introduced.

A condition characterized by vomiting, anorexia and loss of weight is some-times diagnosed as an idiosyncrasy to cow's milk. The diagnosis is made much more frequently in some countries than in others and may not always be justifiable. The truth probably is that idiosyncrasy to cow's milk is uncommon, whereas the injudicious use of cow's milk, undiluted or unsterile or unsuitably modified, is much more common. Even human milk is occasionally implicated as the cause of gastro-intestinal troubles, but the proven cases of sensitivity to human milk are extremely rare (Wergeland, 1948). One case, in which the child developed an eosinophilia of the bone-marrow and blood, was described by Morf (1950).

Gastro-intestinal upsets in children are almost invariably treated by changing the diet, and cow's milk is usually the first constituent to be reduced or omitted. Without going too deeply into the advisability of this procedure, it may be said that it is not always justifiable on scientific grounds. There have, however, been numerous attempts to find a nourishing food to take the place of cow's milk when upsets occur, and milks of vegetable origin or made from mixtures of cereal and meat products have been devised. Some of them have been used for long periods without ill-effects.

Milk Substitutes which have been Used

COW'S MILK AND THE MILK OF OTHER ANIMALS

When a child was deprived of the breast milk of its mother, the use of milk from other animals must have been suggested by analogy, and perpetuated by success. Anyone who has lived in a country where cow's milk is plentiful must find difficulty in realizing that it is really almost as artificial a food for a child as any laboratory mixture. It is not impossible that the milk of other mammals might be more suitable. De Vallambert (1565) advised the use of goat's milk, and Desessartz (1760) discussed the relative merits of the milk of the ass, mare, goat and ewe*; more modern paediatricians have successfully used the milk of asses and mares, in which the concentrations of protein and carbohydrate are a little higher than in human milk, but that of fat is much lower (Freudenberg, 1946, 1948).

In European countries and in the United States cow's milk is the substitute most commonly used. Its composition differs in some important particulars from that of human milk (see Tables 3 and 4, pp. 6, 7). Dilution of cow's milk with an equal amount of water brings its protein content near to that of human milk, as is shown in the fifth column of Table 4, and half milk and half water is the modification most often used for feeding young children. The reduction in calories and carbohydrate which the dilution entails is usually made up with sucrose.

Reference has already been made (p. 9) to the chief differences in amino-acid composition between the milks of the two species. Cow's milk is so superior in amount of total protein to human milk that it should supply, when used as a substitute, sufficient of all the amino-acids and a large surplus of most of them. For this reason, it might in some circumstances be preferable to human milk for feeding premature children (Gordon, Levine and McNamara, 1947).

Cow's milk is a rich source also of calcium and phosphorus. The ratio of

* He spoke also of "quelques Paysans forts et vigoureux, qui néanmoins n'avoient jamais pris d'autre lait que celui des animaux: ces exemples rares et celui même des Moscovites et des Irlandois, où l'usage du lait de femme est exactement inconnu . . ."

calcium to phosphorus is lower than in human milk, and when cow's milk provides the whole diet of a susceptible child, the disturbance of mineral balance may cause tetany (Porter and Carter, 1942; Gardner, MacLachlan, Pick, Terry and Butler, 1950).

The amount of 500 g. which has been taken as the equivalent in cow's milk of 750 g. human milk (p. 9) would provide 750 I.U. vitamin A, 10 I.U. vitamin D, 225 μg. vitamin B_1, 750 μg. riboflavin, and 10 mg. vitamin C. The values are taken from Kon's (1947–8) figures for the average composition of summer milk. Comparison with the values for 750 g. human milk (p. 6) shows the cow's milk to be the richer in vitamin B_1 and riboflavin but the poorer in vitamin C. Cow's milk contains also a growth factor believed to be necessary for rats (Cary and Hartman, 1947), and the factor strepogenin (Woolley, 1946) with similar properties (see p. 22).

SUBSTITUTES BASED ON THE SOYA BEAN

The substitutes for human milk so far considered have been the milks of other animals, but there are large areas of the world where extremely little milk, and very little other food of animal origin, is available for children. In such places milk substitutes of plant origin are of particular importance.

The most successful plant source that has so far been tried extensively is the soya bean (*Glycine max*, L.). It has many advantages. It is not difficult to grow or harvest, and it stores well. It contains much protein with a high proportion of

TABLE 8

Composition of soya beans and soya flours compared with that of dried skimmed milk (from the data of Jolliffe, Tisdall and Cannon, 1950)

Nutrient	Unit	Dried, skimmed milk (per 100 g.)	Whole, mature soya beans (per 100 g.)	Full-fat soya flour (per 100 g.)	Low-fat soya flour (per 100 g.)
Protein	g.	35·5*	34·9	36·0	44·6
Fat	g.	1·1*	18·1	20·7	1·0
Carbohydrate	g.	52·2*	12·0	11·3	14·3
Calcium	mg.	1,300	227	194	267
Phosphorus	mg.	1,035	586	552	623
Iron	mg.	0·6	8	12	13
Vitamin B_1	mg.	0·33	1·14	0·76	1·00
Riboflavin	mg.	2·0	0·31	0·27	0·33
Nicotinic acid	mg.	1·1	2·1	2·3	3·0
Ascorbic acid	mg.	11	Trace	Trace	Trace
Vitamin A or carotene	I.U.	44	111	140	70
Calories		355*	351	373	247

* These figures are higher than those usually given in British tables. McCance and Widdowson (1946) give protein 34·0 g., fat 0·3 g., carbohydrate 49·2 g., and Calories 326.

lysine, and much fat with a high proportion of linoleic acid. Its carbohydrate, although in theory far from ideal, is well tolerated, and does not contain more than a trace of starch. Some analytical data are given in Table 8 and values for dried, skimmed cow's milk are included for comparison. In the Table, the values

for carbohydrate in the soya products are estimates of the amounts that may be available; an uncertain, but undoubtedly large, proportion of the total carbohydrate is indigestible. Compared with skimmed milk, soya has one sixth as much calcium and half as much phosphorus. The ratio of calcium to phosphorus is, therefore, widely different in the two foods.

The one serious disadvantage of soya is that it must be cooked extremely well before it can be digested easily. Failure to recognize the necessity has led to prejudice against the extension of its use. It is probable that the cooking cannot be considered satisfactory unless it results in the destruction of the trypsin inhibitor. In the feeding of small children the possibility of interference with tryptic digestion is of importance because tryptic activity in the intestine of the newborn child is low and remains so for the first 6 months of life (Andersen, 1942; Farber, Shwachman and Maddock, 1943). There have been many trials of soya in children's diets and some of them are summarized in Table 9. In few of the trials were the soya diets compared adequately with milk diets; the trypsin inhibitor was almost certainly present in its active form in most of the diets, and it is clear that the results of the trials must now be regarded as inconclusive. If the results obtained by Lewis and Taylor (1947; see p. 22) are applicable to children, the presence of the inhibitor may have considerably affected the growth of the children. When the intakes of protein and calories from soya diets have been estimated, it has usually been found that high levels were necessary to maintain good growth, but it seems likely that different results might have been obtained if properly prepared soya had been used. The absorption and retention of the nitrogen of soya protein was measured in several of the experiments but, since these results, more than any others, may have been affected by the presence of the inhibitor, their value is uncertain.

Various figures for mineral retentions are perhaps more reliable. Fan, Woo and Chu (1940), whose soya milk was autoclaved, decided that its calcium was as well retained as that in cow's milk, but that the retention of its phosphorus was lower. Desikachar and Subrahmanyan (1949) and Karnani, De, Subrahmanyan and Cartner (1948) found no difference in the utilization of calcium from soya and cow's milk diets. The retention of calcium from commercial soya preparations such as those referred to in Table 9 is about 25 per cent (Schroeder, Cahill and Smith, 1946).

Disadvantages of Soya Preparations

A disadvantage of several of the soya preparations referred to in Table 9 was that they were liable to cause gastro-intestinal upsets. Other writers have reported the same trouble. Platt (1936) had an unfortunate experience in the use of a Chinese soya milk, sold in the native market, and known to the mothers as liable to cause diarrhoea. Stoesser (1944) made a thorough trial of one of the U.S. commercial preparations, similar to No. 9 in Table 9, by feeding 37 children from 2 months to 2 years old on it. Twenty-two of them developed diarrhoea or vomiting. A child given another commercial mixture to which, it is presumed, vitamin A had not been added, developed keratomalacia which led to blindness (Blackfan and Wolbach, 1933).

These disasters, and the less serious but equally undesirable development of rickets which has occurred when the soya diets have contained insufficient calcium or vitamin D, should not be allowed to detract from the potential value of the soya bean in infant feeding if it is properly used. They should instead, stimulate a search for the ideal method of preparation.

TABLE 9

Ingredients and composition of soya preparations, with details of their practical application in child feeding

No. of preparation	Ingredients and method of preparation	Protein (%)	Fat (%)	Carbo-hydrate (%)	Calcium (%)	Phosphorus (%)	Details of use in child feeding, with comments	Authority
1	Beans soaked in water overnight, dehusked and boiled to a gruel, which was strained.						Said to be well taken by children. A soya gruel used by Sinclair (1916) was effective against infantile diarrhoea.	Ruhräh (1909, 1910)
2	Soya flour and twice as much barley flour boiled for 20 min. Condensed cow's milk was added.						Six children of 4–9 months were fed successfully. The proportions of the flours were varied, but if too much soya flour was used, the stools became thin, dark and foul.	Ruhräh (1915)
3	Soya bean protein, lactose and washed butter cooked together.						Used with good effect in eczema and other allergic conditions, but gastro-intestinal upsets were common.	Schloss (1920)
4	Beans soaked in water overnight, dehusked and ground to a paste, which was filtered. The filtrate was boiled for 20 min. before use.	4·4	1·8	1·5	0·018	0·057	One child 5 weeks old who was given the milk for 8 months developed rickets because the calcium content was too low, but otherwise it progressed satisfactorily. The Calorie intake was from 110–130 per kg. body weight.	Tso (1928); see also Tso, Yee and Chen (1928); Tso (1929a, b); Tso and Chu (1930–1, 1931); Chang and Tso (1931)
5	As No. 4, but filtrate was boiled for only 15 min. Cane sugar, egg yolk, sodium chloride and calcium chloride were added, and the mixture was spray-dried.	29·0	16·0				Given to a child 7 weeks old, who grew satisfactorily.	Reid (1934); see also Reid (1935)
6(a)	As No. 4, but filtrate was boiled for 60 min. Cane sugar, bean starch, sodium chloride and calcium lactate were added. The mixture was heated again before use.	2·5	1·6	6·8	0·044	0·030	Given to 15 children from 2–6 months old. Development was good, but 9 children had mild rickets.	Guy and Yeh (1938a)

	Composition						Notes	References
6(b)	Beans roasted and ground. Method otherwise as No. 6 (a).	4·2	1·4	10·2	0·076	0·060	Given with vitamins A, D and C to about 50 children, it seemed to be a complete food.	Guy and Yeh (1938b)
7	Beans roasted and ground. Wheat, sugar, bone meal and sodium chloride were added and the mixture was autoclaved.	4·0	1·9	11·0	0·035	0·065	Theoretically an excellent mixture in the preparation of which the principles of protein supplementation (p. 37) and thorough cooking were combined. Some damage to the protein may, however, have been caused by the roasting.	Fan, Woo and Chu (1940)
8	To a milky fluid obtained from beans 'specially treated to remove unpleasant flavours' (no details given) were added malt syrup, lactose, cottonseed oil, butter fat, cod-liver oil, vitamin C, iron and calcium glycerophosphates, sodium and potassium chlorides, magnesium and calcium lactates. The mixture was homogenized and spray-dried.	14·0	18·0	53·0	0·80	0·50	A mixture devised after detailed consideration of the properties of soya. It was given to about 200 children. As the sole food of children it produced variable gains; older children given it as a supplement to breast milk grew better, but not as well as children given breast and cow's milk. The stools were frequent, bulky and green, and contained large food residues; they improved if the mixture was boiled. The substitution of 7% milk protein for 7% of the soya protein did not seem to improve growth.	Rittinger and Dembo (1932); Rittinger, Dembo and Torrey (1935)
9	Soya flour (61%), arrowroot starch (9%), dextri-maltose (6%), olive oil (19%), dicalcium acid phosphate (4%) and sodium chloride (1%) were mixed with water, homogenized, dried and tinned.	30·0	19·2	37·0	1·48	1·40	A commercial preparation, sold in the U.S., resembling a mixture devised by Hill and Stuart (1929; see also Hill, 1931) which gave good results in infantile eczema. The original mixture contained calcium carbonate but Stearns (1933) advocated the use of dicalcium phosphate instead. Hill's results were confirmed by Ribadeau-Dumas, Mathieu and Willemin (1930) who found, however, that the weight gains were not always satisfactory. Klein (1933) too recommended the mixture, but said children tired of it. For the use of soya in eczema see also Mader (1931) and Becker (1934).	

Table 9 (*continued*)

No. of preparation	Ingredients and method of preparation	Protein (%)	Fat (%)	Carbohydrate (%)	Calcium (%)	Phosphorus (%)	Details of use in child feeding, with comments	Authority
10	Soya flour (12%), soya oil (6%), dextrose and sucrose (5%), soya lecithin (0·2%), calcium phosphate (6·7%), calcium carbonate (0·4%) and sodium chloride (0·4%) were mixed with water (75%), homogenized and canned (tinned).	6·0	7·8	8·9	0·26	0·22	This was another U.S. commercial preparation sold for the treatment of allergic conditions in children. It differed from No. 9 in being a wet material and in having much more fat.	
11	Soya flour was mixed with 5 to 6 times its own weight of water containing sodium bicarbonate, sodium citrate, sodium chloride and disodium hydrogen phosphate (0·1% of each). The salts were used to help in bringing the solids into solution. The mixture was shaken, allowed to stand overnight and filtered. The filtrate was boiled for 15 min.	5·2	2·5	2·9			In a series of trials about 80 children under 4 years old and 60 from 5–10 years old were given the milk. The results could not be treated statistically, but it was considered that the weight gains compared favourably with the gains of similar children given cow's milk.	Report of the Scientific Advisory Board (1947); Desikachar and Subrahmanyan (1949); Pasricha (1950)
12	Equal amounts of soya flour and full-cream, dried milk were mixed together. Sugar and hot water were added but the mixture was not boiled.						Eighty children from 1–5 months old were given the mixture. Their stools were more frequent, and softer, than those of a comparable group given cow's milk without soya; 19% of the soya group, but only 6% of the cow's milk group, failed to gain weight and had gastro-intestinal upsets. The stools improved if the mixture was boiled.	Mackay (1940)

The Preparation of Soya for Food

The use of soya on a large scale probably began in China. Soya curd has been eaten there for many centuries. It is precipitated from an emulsion of the beans with plaster of Paris or with the mother liquor obtained in the manufacture of salt from sea water (Horvath, 1938–9). Guy (1936) referred to a weak solution of the bean that was drunk mostly by adults in Peiping but had been tried after "reinforcement" in the diets of infants, and said also that a preparation of cornflour and soya flour, baked with turnip, was nibbled by weanling children.

For most of the experiments referred to in Table 9 a suspension of the crushed beans was filtered to produce a milk, or a soya flour was used. The various mixtures were used in the wet state, or were dried to a powder resembling dried cow's milk. Soya milks, unfortified, contain little fat. Commercially, three kinds of soya flour are made; in one all the fat is retained, in another one quarter to one half of it is removed by mechanical pressure, and in the third nearly all the fat is removed by continuous solvent extraction. The method used was not specified in any of the descriptions of the experiments, which is very unfortunate because it is now known that the quality of the protein depends on the method of preparation (see p. 18).

The commercial processes vary in detail but, up to the point where the oil is extracted, are essentially the same. After being cleaned, the beans are steamed to remove substances which have a bitter taste. The steaming is interrupted in one process after from 10 to 15 minutes and the beans are dried and cracked; the husks are then removed, and the kernels are ground. The ground material is then steamed again for a further 10 minutes, but it is not usual in any of the processes for the steaming to be carried on for long enough to destroy the trypsin inhibitor.

From a consideration of the various methods, and from the experience of the writer, the following procedure has been evolved for preparing small amounts of soya for infant feeding. The beans are soaked in water overnight and then rubbed to remove the husks, which are washed away with more water. They are then minced, steamed for 2 hours or more, and finally autoclaved (see p. 19). Alternatively they can be steamed for from 8 to 10 hours. The steaming and autoclaving are conveniently done in an ordinary domestic pressure cooker, glass jars of the kind used for preserving fruit being used to hold the minced soya. Prepared in this way, the beans are soft and of good flavour. They can be ground easily into a fine paste which can be incorporated into almost any other food. Diluted with water, the paste makes a thin suspension that passes without difficulty through a feeding tube. The paste usually contains about 17 per cent of protein and 8 per cent of fat. The addition of sugar, sodium chloride and a calcium salt is advantageous.

For feeding very young children, the most suitable preparation is probably a soya milk, made by spray-drying the liquid filtered from soaked, dehusked, ground and autoclaved beans. The product is fine and completely innocuous, but it has the disadvantage of being expensive. The spray-drying is costly and the yield is low. In one batch made for the writer, about 16 lb. of the dried material were obtained from 112 lb. of the raw beans. The sample contained 40 per cent of protein and 7 per cent of fat. It was the first preparation used when the treatment of advanced kwashiorkor with mixtures of plant protein was attempted. It proved successful, and later it was found that the paste made from the whole beans could be used also (Dean, 1952).

In Malaya and Indonesia, soya is rendered digestible by an ingenious method, which is described by van Veen and Schaefer (1950) and by Smith and Woodruff

(1951, p. 192). A fungus, *Aspergillus oryzae*, usually found in association with a species of *Rhizopus*, is sown on a mass of the soaked and dehusked beans and left to grow for 24 hours. It "alters the protein, hydrolyses any starch present . . . and possibly hydrolyses also a certain amount of cellulose". It was fried in deep fat, a method of cooking that might not be the most suitable for small children, but other methods could undoubtedly be devised. The material certainly deserves further investigation because the fungus by its activity might confer great nutritive benefits besides enhancing digestibility and palatability.

OTHER MILK SUBSTITUTES OF PLANT ORIGIN

Preparations based on materials other than the soya bean have been used from time to time in place of cow's milk. Fischer (1914a, b) said that almond and peanut milks were valuable in the treatment of gastric upsets as well as of cow's milk allergy. He mentioned that such milks made a finer curd than cow's milk and were more rapidly digested.

Almonds

Chapin and Kast (1918) recommended for children the use of almond milk made by grinding the nuts finely, adding water and standing the paste overnight in the ice-box. The paste was poured through gauze, and the resulting fluid contained, per cent, protein 3·3 to 4·4, fat 5 to 7, and carbohydrate 0·9 to 1·2. Their experience was not, however, entirely favourable. Three of their subjects were sick children from 2 to 3 months old; they were losing weight, and the almond milk did not check the loss. A few older children took the milk satisfactorily, but an equal number tired of the taste. Hess (1932) seems to have been more fortunate in his use of almond milk for infantile eczema. He did not use it alone, but with rice meal and sugar, meat broth and yeast, and with semolina. Ujsághy (1939, 1939–40) compared the absorption and retention of nitrogen and sulphur by infants from 2 to 4½ months old when given almond milk, a mixture of cow's milk and rice water, and human milk. The absorption and retention were about the same with the first two diets but were slightly higher with the human milk.

Coconut

Gesteira and Bahia (1932) treated more than 50 children suffering from gastro-intestinal disturbances with a milk obtained from macerated coconut. They considered it a useful therapeutic agent.

Sunflower Seeds

The only real rival to soya that has so far received an extensive trial in child feeding as substitute for cow's milk is meal made from the seeds of the sunflower plant (*Helianthus annuus*, L.). The seed kernels have the percentage composition: protein 27, fat 45, carbohydrate 14 (Platt, 1945). The use of sunflower seed meal was described by Willemin-Clog (1930) and by Ribadeau-Dumas, Mathieu and Willemin (1930). Their work is referred to by André (1928) in his survey of the nutritive value of the oil-bearing seeds. The meal was prepared from the decorticated and defatted seeds. If it was used by itself, the infants grew well for about 3 weeks, but for good and continuous weight gains, supplements were necessary. A satisfactory mixture incorporating the meal had 10 parts cream of rice, 5 parts sugar, 2½ parts malt extract, 4 parts sunflower meal, 2 parts sodium chloride and 4 parts calcium carbonate. The rice, sunflower meal and sodium chloride were put into cold water and heated until the volume was reduced by a third.

The mixture was allowed to cool, the malt was added, and after the solution had cleared it was boiled for 1 minute. The sugar, sometimes with some butter fat, was added and the milk was ready for use. It was advised that when possible a little sweetened condensed cow's milk or yeast should be included. About 130 children aged from 10 weeks to 10 months were treated for cow's milk intolerance, eczema and dyspepsia by using the mixture in their diets. The results were said to be good; the stools were not greatly increased in number, but were bulky, variously coloured and had a characteristic smell. The utilization of nitrogen was high. Later, in discussing the conditions in which substitutes for milk may be necessary, Ribadeau-Dumas (1946) re-affirmed his belief in the value of sunflower meal, but pointed out that, although the amino-acid mixture in his suggested diet was apparently adequate, he had discovered that about 20 per cent of its protein was needed to give rat growth as good as that supported by 5 per cent of lactalbumin. He advocated the addition of autoclaved yeast and gave it as his opinion that the vegetable preparations were probably best thought of as milk sparers; they had a good supplementary effect when given with milk. He suggested tentatively that inclusion of some fat of animal origin might be necessary for complete success. Other writers (Jacquot, 1944; Day and Levin, 1945; Grau and Almquist, 1945; Mitchell, Hamilton and Beadles, 1945) realized the importance of finding out the best way to prepare the sunflower meal, and Jacquot expressed his fears that its high silica content might be a disadvantage.

Groundnuts, Peanuts

Desikachar, De and Subrahmanyan (1948a) realized the potential value of milks made from coconuts, cashew nuts and groundnuts (peanuts), and investigated the last-named in rat experiments. Groundnuts (*Arachis hypogaea*, L.) have the percentage composition: protein 23, fat 47 and carbohydrate 10 (Platt, 1945). The kernels of the nuts were separated from the skin and ground to a fine powder. Water was added, and the mixture was boiled and strained through cloth. The reaction of the milk was adjusted to pH 4, otherwise it curdled rapidly. By another method of preparation the nuts were germinated so that the biological value of their protein was improved and supported better weight gains. Calcium may have been a factor limiting growth in these experiments. The milk was considered worthy of trial in infant and child feeding.

More detailed and precise instructions for preparing a groundnut milk were given by Moorjani and Subrahmanyan (1950). The nuts were germinated and yielded finally a thick white product "reminiscent of buffalo milk in appearance", and of pleasant flavour. Its percentage composition was: protein 3·3, fat 4·2 and carbohydrate 2·9, but the ash was only 0·3. The milk curdled when even very small amounts of calcium were added. The difficulty was overcome by adjusting the pH to 6·6 with sodium bicarbonate, and adding sodium citrate and disodium phosphate, followed by calcium gluconate. The milk then contained 61 mg. calcium per 100 ml. It was not tested on human subjects, but experiments showed that 31 per cent of its calcium, and 34 per cent of its phosphorus were retained; from cow's milk, given in the same conditions, 34 per cent of the calcium and 39 per cent of the phosphorus were retained. Moorjani, Subrahmanyan and Satyanarayana (1950) have more recently reported favourably on a milk made from 3 parts of groundnuts and 1 of soya bean, both of them germinated, and fortified with calcium. The milk was not as effective as cow's milk in supplementing a "poor rice diet" for rats, but it may have been that not enough calcium was added. No advantage was seen of adding malted barley to the mixture.

Rice Water

Another substance of a milk-like nature which, it was thought, might profitably be used in child feeding was the water in which unpolished rice has been cooked (De, Desikachar, Dudani, Karani and Subrahmanyan, 1947). It is usually thrown away but contains valuable amounts of soluble protein and vitamins of the B complex. On cooling it was said to form a kind of gruel which hindered cooking when the material was incorporated into other dishes; the gruel was, moreover, penetrated with difficulty by the digestive juices. In spite of the disadvantages it was recommended that the gruel should be made into a pudding by boiling it with white wheat flour, sugar and salt. It was reported that trials of the pudding for feeding schoolchildren were in progress in Bangalore.

Mixed Plant Sources

Finally, mention must be made of some work which seems to be an excellent advertisement for vegetarianism. Lane and Bosshardt (1930) compared the growth and well-being of two groups of 13 orphanage children, from 7 to 15 years of age. The diets of both groups provided between 50 and 60 g. protein a day, but in one about 30 g. were from animal sources and in the other none. The diet of the first group included milk and provided about 1 g. of calcium daily; that of the other group contained less, about 0·5 g. The authors were aware of the importance of minerals, but they were able to state "there appears no reason to conclude that a scientifically balanced milk diet, including $1\frac{1}{2}$ pints to 1 quart of milk per day per child, produces greater growth or better health in growing children from 7 to 15 years old than a scientifically chosen vegetable diet furnishing a smaller amount of calcium".

Lane (1931) produced also an interesting study of a woman who lived on a diet almost exclusively of vegetable origin throughout a pregnancy and gave birth to healthy twins weighing 6 lb. 9 oz. and 6 lb. 4 oz.; "occasionally a little cream, an egg and a small serving of meat once a week" were the only foods of animal origin which the woman ate. Her diet provided less than 2,000 Calories a day and about 0·65 g. of calcium. Her children were fed at first on breast and cow's milk, but the latter was gradually replaced by a vegetable milk. No cow's milk was given after 3 months, and after 5 months, when breast feeding stopped, the vegetable milk was the only milk used. It was made from unblanched ground almonds (12 parts), unroasted peanuts (2 parts), whole wheat flour (2 parts), shorts (1 part), soya flour (4 parts; its preparation was not described), and corn starch (2 parts). The materials were boiled with vegetable water (from celery, chard, lettuce, carrots or beans) for 3 minutes and sugar and salt were added. The milk was kept on ice. Cod liver oil and orange juice supplied vitamins A, D and C. The milk, as given to the children, contained, per cent, protein 2, fat 4, and carbohydrate 8. It was the children's sole diet between the ages of 5 and $8\frac{1}{2}$ months, and they grew well. They continued to thrive on an entirely vegetable diet for the whole period of observation which lasted in all for nearly 3 years.

SUBSTITUTES COMBINING PLANT AND ANIMAL SOURCES

A number of artificial milks which have been used from time to time fall between the purely vegetable and the natural animal product, because they contain ingredients of both kinds. Cadogan (1753) strongly favoured breast feeding, but if it was impossible, he advised, "that one half of Infants Diet be thin light Broths, with a little Bread or Rice boiled in them; which last is not so acescent as any other kind of Meal or Flour. . . . The other Part of Childrens

Diet may be a little Bread and Water boil'd almost dry, and then mix'd with fresh Milk not boiled." The broths should be made of animals' flesh, because "as we are partly carniverous Animals, a Child ought not to be fed wholly upon Vegetables. The Mother's Milk, when it is perfectly good, seems to be this true Mixture of the animal and vegetable Properties, that agrees best with the Constitution of a Child."

Desessartz (1760) mentioned the value of malt flour in infant feeding; he thought the various processes which had been involved in its making had altered it, as cooking might alter it, into an easily digestible material. If malt flour could not be obtained, "*de mie de pain*" should be used instead. This was the "pap" of bread, soaked and sometimes boiled in water, which was condemned by Underwood (1784), another great advocate of natural feeding. In his view, if cow's milk had to be used, a jelly of hart's horn shavings should be incorporated and a little Lisbon sugar. In spite of his condemnation, "pap" continued to be used. It was still popular 70 years later, when Liebig (1869) announced that the slight modification introduced by malting the cereal "converted it into a perfect nutrient". "The missing potash" and other phosphates had to be provided, "and a number of facts show most indubitably that this soup, without any additional food, nourishes children admirably". Four years earlier, Liebig (1865) "with that remarkable estimation of the greatness of small things which is one of the most valuable of his many high intellectual qualities, and with a tender appreciation of the importance of small people" (Editorial, 1865), had introduced his famous infant food in which starch of wheaten flour had been "transformed into the soluble forms of sugar and dextrine. This he effects by adding to the wheaten flour a certain quantity of malt". The "unnecessary labour in the organization" which was imposed by the feeding of the starch was thus spared. The recipe for the "soup" was: "half an ounce of wheaten flour, and an equal quantity of malt flour, seven grains and a quarter of bicarbonate of potash, and one ounce of water, are to be well mixed; five ounces of cows' milk are then to be added, and the whole put on a gentle fire; when the mixture begins to thicken it is removed from the fire, stirred during five minutes, heated and stirred again till it becomes quite fluid, and finally made to boil. After the separation of the bran by a sieve, it is ready for use. By boiling it for a few minutes it loses all taste of the flour." The soup was said to have given excellent results with infants, including two of Liebig's own grandchildren, for one of whom it was originally devised. Some French investigators reported unfavourably, but they were said to have used unsuitable malt and otherwise to have failed to follow the instructions carefully; echoes of a furious Continental controversy over the value of the food were to be detected in *The Lancet* for several years. English opinion seemed on the whole to be favourable. The virtue of Liebig's food resided presumably in its mixture of cereal proteins with those of cow's milk, and its maltose and other sugars which replaced the cereal starch. Liebig's claim for the advantage of his treatment of "pap" was perhaps an excess of enthusiasm, although it is not impossible that some benefit may have been conferred by adding the malt flour. Malt flour does not contain the amylase inhibitors which are found in many cereals (Kneen and Sandstedt, 1943), but their importance in human nutrition has not yet been established.

Subsequent attempts by many workers to produce an artificial milk were never really successful, although they were based on analyses of milk for its protein, fat and carbohydrate, and although concentrated and dried cow's milk had become available. Friedenthal (1910, 1914) decided to re-investigate

the problem with special reference to the mineral content and the physical and chemical characteristics of human milk, which had previously been largely neglected. His milk, in addition to a mixture of salts, contained cow's milk protein, lactose and butter fat. It was given an extensive clinical trial, with good results, by Bahrdt (1914). A modification proposed by Schloss (Müller and Schloss, 1914), in which the lactose was replaced by a mixture of maltose and dextrin, was successful also. Gerstenberger, Haskins, McGregor and Ruh (1915) returned to Friedenthal's original formula, but substituted other fats, such as a mixture of lard and coconut oil, for the butter, in order that the fat in the final product should resemble in its physical and chemical characteristics the fat of human milk, which had recently been more fully analysed. The mixture of fats chosen had a small proportion of glycerides of low volatile fatty acids and the saponification number, iodine number and other characteristics were nearly identical with those of human-milk fat. The food was homogenized, which involved heating under pressure, although Friedenthal had advised against heating skimmed cow's milk. It was well digested by infants.

Hindes (1926), writing from Baku, said his 20 years' experience of infant feeding had convinced him that children could be reared successfully for long periods on diets containing no human or cow's milk. He referred to the use by other workers of such materials as a mixture of liver broth, rice water and wheat flour with olive oil; broth made from calf bone-marrow; rice puddings made with eggs and various decoctions of rice. He advocated proteins from animal and vegetable sources, recognized the need for adequate minerals, and believed that if the fat in the diet was insufficient, a toxic substance was formed through the incorrect utilization of protein. He himself used a food made from groats, wheat flour, malt syrup, vegetable water, egg white and bone-marrow. The mixture was incorporated to suit the tastes and needs of children of different ages, in *Brei*, soups, purées and puddings. Abraham (1928) gave details of a somewhat similar diet made by stirring up *Zwiebackmehl*, of which the composition was not given, in water, adding egg yolk, sugar, butter and salt, and cooking on a water bath. It was said to give good results in infant feeding.

UTILIZATION OF THE MALTING PROCESS

It is obvious from the foregoing account of early trials of malted materials that the possibility of utilizing the principles of malting in preparing diets for infants has been realized for a great many years. Essentially, the technical processes have remained unchanged; the best conditions have been defined and can now be attained independently of external temperature and humidity. The first step is the germination of the cereal.

During the process of germinating the cereal, enzymes are formed and liberated, and there is some degradation of proteins and starch to simple diffusible substances (Hopkins and Krause, 1937). After germination the malt contains about 50 per cent starch and the percentage of sugars formed at this stage is maltose 1·3 to 5, sucrose 2·8 to 6, glucose 1·3 to 3, and fructose 0·7 to 1·5 (Ross-Mackenzie, 1935). The percentage of total protein is about 10·0, but it also is subject to wide variations. Water is added and the suspension, known as the "mash", is heated to the optimum temperature for enzyme action. The chief processes which then affect the carbohydrate are the liquefaction of the starch paste by an amylo-phosphatase or an alpha-amylase, the conversion of starch to dextrins by means of alpha-amylase, and the hydrolysis to maltose by

beta-amylase of more starch and the dextrins. The second and third processes go on simultaneously, but the ratio of the amounts of dextrin and maltose produced varies with the conditions provided. Mashing causes also some further splitting of the protein.

The final process in the commercial method is the extraction of water. A typical malt extract has about 70 per cent solids; when dried it has the following composition (Marshall, 1949):

		Per cent
Maltose ..	..	61·60
Glucose ..	..	9·45
Sucrose ..	..	1·74
Dextrin .. `	..	7·36
Protein ..	..	7·87
Other nitrogenous		
substances	..	6·62
Minerals ..	..	1·46
Moisture..	..	3·90

The percentage of glucose can be doubled.

A modification of the malting process, by which hot air is blown through a mixture of malt flour and cereal flour, was described by Hesse (1948). The percentage of maltose obtained depended on the duration of the process, and on the amount of malt flour present. The condensation of water on the particles of flour at a temperature of from 40° to 50° C. provided the right conditions for amylase activity, but the finished product was quite dry. It was used successfully for feeding children.

CONCLUSIONS

The future of milk substitutes made from plant materials would seem to depend on the use of a cheap, highly concentrated source of plant protein. At the moment, the practical choice lies between soya beans and sunflower seeds, but there may be other possibilities such as legumes, nuts and seeds, usually grown for their oil, but which after the extraction of the oil provide a very nutritious cake. Examples are groundnuts and cottonseed, the cake from which has already become a valuable cattle food.

It is obvious from the experience here summarized that much thought must be given to the methods of processing new foods. When the best methods have been determined, it will be possible to begin in earnest to exploit the possibility of combining plant proteins, which forms the subject of the next section.

The Supplementation of Plant Proteins

ISOLATED PROTEINS

Proteins that are obtained from plants by the ordinary methods based on differences of solubility may be a collection of various protein fractions (Block, 1933; Vickery, 1945; Briggs and Mann, 1950). They may even be artefacts; there is little knowledge of the state in which proteins exist in living tissue, and of the extent to which they are altered by the process of isolation (McCollum, Orent-Keiles and Day, 1939). It is even possible that, in the course of isolation, enzyme-resistant linkages may be produced among the amino-acids. Zein

predigested with enzymes appears to be much inferior as a dietary supplement to zein hydrolysed by acids (Geiger and Hagerty, 1949). The isolated proteins have, however, been shown to have a relatively constant amino-acid composition which can be determined somewhat more easily than that of a mixture of proteins, because, in the process of isolation, carbohydrate, which is one of the chief causes of difficulty, has usually been removed more or less completely.

Any single protein is likely to be inadequate for growth or maintenance and observation of the effects of adding various amino-acids sometimes provides valuable information. Thus Osborne and Mendel (1914) fed rats on gliadin, isolated from wheat, and the rats failed to grow. When lysine was added, growth was excellent, but when it was withdrawn, growth stopped. In the same way, the zein of maize was found to be inadequate alone; the addition of tryptophan was needed to maintain weight, but for growth lysine had to be added as well. No growth was obtained with diets having equal amounts of gliadin and zein, which was explicable on the ground that both proteins lacked sufficient lysine. Osborne and Mendel pointed out that the addition of the amino-acids could theoretically be accomplished by giving them in the form of proteins, and offered a practical demonstration by replacing a quarter of the zein in a diet, in which it was the only protein, by lactalbumin. Growth was excellent because of the lysine and tryptophan which were brought in.

A similar experiment showed that the arachin of the groundnut, providing 15 per cent of protein as the sole source of nitrogen in the diet, allowed growth of rats only at the very small rate of 0·23 g. daily (Beach and White, 1937).

TABLE 10

Amino-acids needed to supplement various plant foods effectively as shown by animal feeding experiments, together with the amounts of lysine, cystine and methionine in the foods

Food	Content of :			Supplementary amino-acids needed for rat growth†	Authority
	lysine (g./16·0 g. nitrogen)*	cystine (g./16·0 g. nitrogen)*	methionine (g./16·0 g. nitrogen)*		
Maize, whole ..	2·0	1·5	3·1	Lysine and tryptophan	Marais and Smuts (1940a)
Oats, whole, hulled	3·3	1·8	2·4	Lysine	Mitchell and Smut (1932)
Rice, polished ..	3·2	1·4	3·4	Lysine and methionine	Kik (1940)
Rye, whole	4·2	—	1·3	Lysine	Johnson and Palme (1934)
Wheat, white flour	2·0	1·9	1·5	Lysine	Light and Frey (1943
Wheat, whole ..	2·7	1·8	2·5	Lysine	Mitchell and Smut (1932)
‡Lima bean (*Phaseolus lunatus*)	—	—	—	Methionine	Russell. Taylor, Mehrhof and Hirsc (1946)
‡Haricot bean (*Phaseolus vulgaris*) ..	—	—	—	Methionine	
‡Soya bean	5·8	1·9	2·0	Methionine	Hayward and Hafr (1941)

TABLE 10 (*continued*)

Food	Content of:			Supplementary amino-acids needed for rat growth†	Authority
	lysine (g./16·0 g. nitrogen)*	cystine (g./16·0 g. nitrogen)*	methionine (g./16·0 g. nitrogen*)		
Chick pea (*Cicer arietinum*)	—	—	—	Methionine	Russell *et al.* (1946)
‡Cow pea (*Vigna sinensis*)	—	—	—	Cystine	Finks, Jones and Johns (1922)
Field pea (*Pisum sativum*)	5·0	1·2	1·0	Methionine	Woods, Beeson and Bolin (1943)
Groundnut, peanut (*Arachis hypogaea*)	3·0	1·6	1·2	Methionine§	Grau (1946)
‡Lentil (*Lens esculenta, Moench.*) ..	—	—	—	Cystine	Jones and Murphy (1924)
‡Cottonseed meal ..	2·7	2·0	2·1	Lysine and methionine	Grau (1946)
Linseed meal ..	2·5	1·3	3·1	Cystine	Smuts and Marais (1938b)
Sesame meal ..	2·8	1·3	3·1	Lysine§	Grau and Almquist (1944)
				Cystine	Marais and Smuts (1940c)
Tobacco seed oilmeal	—	—	—	Lysine	Rapp, Skinner and McHargue (1946)
Lucerne, alfalfa ..	4·9	1·6	2·3	Cystine	Smuts and Marais (1938a)
Potato	—	—	—	Cystine	Beadles, Braman and Mitchell (1930)
Yeast	7·5	1·0	1·9	Methionine	Klose and Fevold (1945)

* From Block and Mitchell (1946–7).

† In some of the papers cited, it was stated that cystine *and* methionine were needed for effective supplementation. As methionine can apparently replace cystine in the diet of the rat, reference to cystine has in those cases been omitted. Where cystine is said to be the amino-acid required, methionine can almost certainly be substituted.

‡Effects of supplementation complicated by presence of heat-labile trypsin inhibitor, or by other necessity for heating (see p. 17).

§Data obtained from chick growth experiments.

When DL-methionine was added, weight increased at the rate of 1·7 g. daily. L-Cystine did not have the same effect. Arachin was investigated also by Baernstein (1937–8). He confirmed that DL-methionine was an excellent supplement, but showed that if tryptophan was added as well the weight gains were still greater. The gains were, however, less than those that followed the addition of casein. The inference was that the casein supplied some other necessary amino-acid, but further experiments showed that it was not lysine or cystine. In the light of present knowledge, it seems possible that the missing substance was not an amino-acid but a growth factor (p. 22).

TABLE 11

The value of combining various foods containing protein. Results obtained, unless otherwise indicated, from rat feeding experiments

No. of food item	Basic food item	Supplementary food	Amount of total protein provided by supplementary food (%)	Total amount of protein in diet (%)	Protein efficiency ratio*	Biological value* Found	Biological value* Calculated	Other results and comments	Authority
1	Maize meal, white	Food yeast	16	8	1·75				Sure (1948)
		Dried buttermilk	16	8	1·70				
		Soya bean flour	16	8	1·66				
		Skimmed milk solids	16	8	1·64				
		Peanut (groundnut) meal	16	8	1·21				
2	Maize	Pea	33	9				Poor growth	McCollum, Simmonds and Parsons (1921b)
		Haricot bean	33	9				Poor growth	
		Rolled oats	50	9				Poor growth, but better than when oats provided 66 % of the protein	
		Soya bean	33	9				Better growth than on maize or soya alone	
		Wheat	33	9				Poor growth	
3	Maize, yellow	Soya bean	45	8		75	61		Marais and Smuts (1940b)
		Lucerne (alfalfa)	45	8		80	64		
4	Maize	Milk	25	10		76	67		Mitchell (1923–4b)
5	Maize	Soya bean	50	10		66		Possibly a supplementary effect, as biological value of maize alone was found to be 58	Mitchell and Villegas (1923)
		Coconut meal	50	10		58			
6	Maize	Soya bean meal	33	9	1·76			Considered to be a true supplementary action	Maynard, Fronda and Chen (1923)
		Rice bran	33	9	1·63				
		Peanut (groundnut) meal	33	9	1·46				

No.					P.E.R.	Biol. value		Reference
	maize, whole, yellow	Tomato seed press cake / Coconut meal	25 / 20	13 / 12				Jones, Finks and Johns (1923)
8	Barley	Soya bean / Pea / Haricot bean	33 / 33 / 33	9 / 9 / 9			Good growth, better than with barley or soya alone / Poor growth / Fairly good growth	McCollum, Simmonds and Parsons (1921b)
9	Oats, rolled	Pea / Soya bean / Haricot bean	33 / 33 / 33	9 / 9 / 9			Fairly good growth, better than with oats or peas alone / Fair growth / Poor growth, but better than with oats alone	McCollum, Simmonds and Parsons (1921b)
10	Oatmeal	Peanut (groundnut) meal	50	8		81 / 77		Smuts and Marais (1938a)
11	Poor south Indian rice diet	Lucerne (alfalfa), dried				The weekly growth rate was almost doubled when 10% of the rice was replaced by dried lucerne.	The diet consisted of rice about 75%, dhal 5%, vegetables, tamarind, chili, groundnut oil, salt and a little, less than 1%, whole milk powder.	Subrahmanyan and Sur (1949)
12	Rye, flour, 70% extraction	Soya bean flour, Berczeller process	62	8	2·43		The rye and soya were made into bread with about 2% yeast. Growth was better than with a plain rye bread or the soya flour alone.	Kon and Markuze (1931)
13	Rye	Soya bean / Haricot bean / Pea	33 / 33 / 33	9 / 9 / 9			Poor growth / Poor growth / Poor growth	McCollum, Simmonds and Parsons (1921b)
14	Wheat	Maize / Sunflower } together	25 / 45	9			Mice. The mixture was made into bread. Growth was as good, after 30 days, as with a control diet containing milk. Sunflower was considered a good supplement to maize.	Csáky (1947)

* Protein efficiency ratio is defined as the g. increase in weight per g. protein eaten. For a full explanation of the term, "biological value", and a discussion of the various methods used in calculating it, see Boas-Fixsen (1934–5), Beach (1948) and Allison (1949).

TABLE 11 (continued)

No. of food item	Basic food item	Supplementary food	Amount of total protein provided by supplementary food (%)	Total amount of protein in diet (%)	Protein efficiency ratio*	Biological value* Found	Biological value* Calculated	Other results and comments	Authority
15	Wheat flour	Peanut (groundnut) flour Meat muscle protein	30 30	10 10				Growth was the same with both supplements, but the amount of peanut (groundnut) protein eaten was slightly greater than the amount of meat protein.	Eddy and Eckman (1923)
16	Wheat flour	Skimmed milk solids, 6% Full fat soya flour, 5·56% Skimmed milk, 3%, soya flour, 2·78%	20 20 20	8 8 8		59 63 62	59 59 59	The milk protein may have been of inferior quality because of loss of lysine during storage. The flour was made into bread with the supplements.	Henry and Kon (1949)
17	Wheat flour, white	Soya bean meal Low-fat wheat germ Skimmed milk solids Maize meal	44 40 39 32	10 10 10 10	2·06 1·99 1·77 1·52				Hove, Carpenter and Harrel (1945)
18	Wheat flour, white	Soya bean meal Skimmed milk solids Peanut (groundnut), cottonseed and soya bean meal Peanut (groundnut) meal Cottonseed meal	35 28 33 34 32	9 9 9 9 9	2·16 1·86 1·40 1·32 1·29			In these experiments 90 parts of the wheat and 10 parts of the supplements were used. Other proportions were tried but were considered to be less economical.	Jones and Divine (1944)
19	Wheat	Millet	33	9				Poor growth	McCollum, Simmonds and Parsons (1919)
20	Wheat flour, enriched	Skimmed milk solids Food yeast Soya bean flour	11 11 11	8 8 8	1·28 1·22 1·03				Sure (1948)

No.	Supplement	Food	%	%	P.E.R.			Growth notes	Reference
22	Pea	Pea Soya Rolled oats	33 33 33 50	9 9 9 9				Good growth Very good growth Fair growth, better than when oats provided 66% of the total protein	McCollum, Simmonds and Parsons (1921b)
	Pea	Barley, pearl Wheat, whole Maize, whole, yellow	50 50 50	10 10 10	1·98 1·80 1·78				Murray (1948)
23	Pea	Wheat germ Maize germ	50 50	10 10	1·96 1·97			The protein efficiency ratio of pea alone was 0·95. A supplement of 0·2% methionine was superior to either of the cereal germs.	Beeson, Lehrer and Woods (1947)
24	Pea	Potato Millet	33 33	9 9				Growth better than on peas alone Good growth	McCollum, Simmonds and Parsons (1921b)
25	Cottonseed meal	Lucerne (alfalfa)	50	10		68	64		Nevens (1921)
26	Cottonseed meal	Soya bean meal	50	11		77	60		Draper and Evans (1944)
27	Flaxseed meal	Rye Rolled oats, millet, cottonseed meal, barley, maize, soya bean	66 66 (each)	9 9				Growth better than with 8% milk protein Poor growth	McCollum, Simmonds and Parsons (1919)
28	Sesame meal	Soya bean, autoclaved	65	10	2·17			The autoclaved soya bean alone had a protein efficiency ratio of only 1·73.	Chang and Murray (1949)
29	Potato	Ground wheat Pea Rolled oats Maize Millet	66 66 66 66 82	9 9 9 9 11				Good growth Good growth, much better than on peas alone Better than oats alone, inferior to wheat with potatoes Fairly good growth Growth poor, but better than with 9% millet protein	McCollum, Simmonds and Parsons (1921a)

* Protein efficiency ratio is defined as the g. increase in weight per g. protein eaten. For a full explanation of the term, "biological value", and a discussion of the various methods used in calculating it, see Boas-Fixsen (1934–5), Beach (1948) and Allison (1949).

Arachin is the chief protein of the groundnut. Its other important protein is conarachin, and as a source of protein for rats the two together are more effective than arachin alone (Baernstein, 1937–8). The reason is found, at least in part, in the content of the sulphur-containing amino-acids; arachin has 0·67 per cent methionine and 1·51 per cent cystine, but conarachin has 2·12 per cent methionine and 2·92 per cent cystine (Brown, 1942).

THE EFFECTS OF SUPPLEMENTING WHOLE FOODS

The results of some rat growth experiments, which have shown the value of supplementing various foods with pure amino-acids, are given in Table 10. Where possible, the figures of Block and Mitchell (1946–7) for the amounts of lysine, cystine and methionine in the proteins of the foods have been included.

KEY TO TABLE 11

The key relates the foods shown in a supplementary capacity to one another

Food item	No. of food items shown in a supplementary capacity
Barley	8, 22, 27
Coconut meal	5, 7
Cottonseed meal	6, 18, 25, 26, 27
Cow's milk	1, 4, 16, 17, 18, 20
Flaxseed meal	27
Haricot bean	2, 8, 9, 13, 21
Linseed meal	6
Lucerne (alfalfa)	3, 11, 25
Maize	1–7, 14, 17, 22, 27, 29
Maize germ	23
Millet (*Sorghum vulgare*)	19, 24, 27, 29
Oats	2, 9, 10, 21, 27, 29
Pea (*Pisum sativum*)	2, 8, 9, 13, 21, 22, 23, 24, 29
Peanut (groundnut)	1, 6, 10, 15, 18, 20
Potato	24, 29
Rice	6, 11
Rye	12, 13, 27
Sesame meal	28
Soya bean meal	1, 2, 3, 5, 6, 8, 9, 12, 13, 16, 17, 18, 20, 21, 26, 27, 28
Sunflower seed meal	14
Tomato seed meal	7
Wheat	2, 14–22, 29
Wheat germ	17, 23
Yeast	1, 20

The Table shows that cereals are usually poor in lysine, but richer in methionine, and that beans, peas and pulses are usually rich in lysine, but poorer in methionine. It would seem obviously beneficial to put the two classes of food together. The suggestion was originally made on the basis of work, which was largely empirical, by Osborne and Mendel (1914), and results which have been achieved by setting foods together are summarized in Table 11.

Some of the analytical data supplied by Block and Mitchell (1946–7) have been rearranged in Table 12 to provide a rapid guide to the theoretical possibilities

of using the supplementary properties of plant proteins in human nutrition. Human milk has been set in the middle of the Table as representing the baseline of amino-acid composition, and the values for the other foods have been placed in order above and below the line, according to whether they contain, respectively, more or less of the given amino-acid than human milk. By using the Table, it should not be difficult to assess the value of many combinations of foods, and of a particular supplement to any one food. If it is desired to express the amount of any amino-acid quantitatively, the amount can be calculated very simply, because all Block and Mitchell's data are for g. amino-acid per 16·0 g. nitrogen.

Table 12 shows clearly the value of cow's milk when added to other foods, not only as a source of lysine and methionine but also of other amino-acids. Thus, the results of analysis are in agreement with the data from rat experiments given in Table 11 and with other data obtained from experiments with children (p. 48). It is worth noting that sardine meal, which has been included in the table as a representative of the fish proteins, is, like cow's milk, a rich source of lysine. It is apparent also how remarkable the protein mixture in human milk is with its high concentration of cystine, tryptophan, lysine and valine (p. 4).

The value of many animal proteins, besides milk, as supplements to proteins of plant origin has been investigated in considerable detail. One of the earlier studies, in which rats were used, was that of McCollum, Simmonds and Parsons (1921c) and since then innumerable trials have been made of the effects of adding such materials as meat scraps and fish solubles to the diets of farm animals. In general, animal proteins are relatively expensive, and their use in human diets is largely determined by economic circumstances (Orr, 1928; Widdowson, 1947). The main theme of the present Report is the search for a cheap substitute for milk and they have not, therefore, been considered in detail. Cow's milk has been included as the obvious exception.

Human Experiments in Protein Supplementation

There have been few experiments with human subjects which have been specifically designed to show supplementary effects of the proteins in foods.

Albanese, Snyderman, Lein, Smetak and Vestal (1949) fed children from 3 to 7 months old on diets devoid of milk containing zein and maize gluten with added lysine and tryptophan, and wheat gluten with added lysine. The wheat gluten produced the best weight gains and the most consistent retention of nitrogen. Hoffman and McNeil (1949), who fed adult hospital patients on diets in which nearly all the nitrogen was derived from wheat gluten, found that, when lysine was added, the total nitrogen requirement was lowered. Murlin, Edwards, Hawley and Clark (1946) found in adult subjects that the biological value of soya protein, derived from a "baked and defatted" soya flour, was usually decreased by addition of individual amino-acids though the nitrogen balance might be improved. There have been a few other experiments with soya; Holmes (1920) gave men diets in which the protein was derived from bread and either peanut or soya bean flour, and concluded that, used in this way, both were valuable foods. Rubner (1928) obtained a good positive nitrogen balance in one adult with a soya-rye bread as the sole source of protein. Kapfhammer and Habs (1930) found that they could maintain positive nitrogen balances on diets providing from 7 to 9 g. of nitrogen daily, of which from 50 to 60 per cent were derived from soya. Bricker, Mitchell and Kinsman (1945) investigated a mixture of soya flour and white flour; the biological value of its protein (55) proved to be

Content of twelve amino-acids, expressed as g. per 16·0 g. nitrogen, in various human milk (Block and

Arginine
- Peanut (groundnut) 9·9
- Sesame seed 9·2
- Peas, garden 8·9
- Linseed 8·4
- Sunflower seed 8·2
- Maize germ 8·1
- Cottonseed 7·4
- Sardine meal 7·4
- Rice, white 7·2
- Soya bean 7·1
- Egg, whole 6·4
- Oats, rolled 6·0
- Wheat germ 6·0
- Maize, whole 4·8

Human milk 4·3
- Lucerne (alfalfa) 4·3
- Cow's milk 4·3
- Rye, whole 4·3
- Yeast 4·3
- Wheat, whole 4·2

Histidine
- Maize germ 2·9

Human milk 2·8
- Yeast 2·8
- Cow's milk 2·6
- Cottonseed 2·6
- Wheat germ 2·5
- Sardine meal 2·4
- Soya bean 2·3
- Maize, whole 2·2
- Oats, rolled 2·2
- Lucerne (alfalfa) 2·1
- Peanut (groundnut) 2·1
- Egg, whole 2·1
- Wheat, whole 2·1
- Sunflower seed 1·7
- Rye, whole 1·7
- Rice, white 1·5
- Linseed 1·5
- Sesame seed 1·5
- Peas, garden 1·2

Lysine
- Sardine meal 7·5
- Cow's milk 7·5
- Yeast 7·5

Human milk 7·2
- Egg, whole 7·2
- Maize germ 5·8
- Soya bean 5·8
- Wheat germ 5·5
- Peas, garden 5·0
- Lucerne (alfalfa) 4·9
- Rye, whole 4·2
- Sunflower seed 3·8
- Oats, rolled 3·3
- Rice, white 3·2
- Peanut (groundnut) 3·0
- Sesame seed 2·8
- Wheat, whole 2·7
- Cottonseed 2·7
- Linseed 2·5
- Maize, whole 2·0

Tyrosine
- Maize germ 6·7
- Lucerne (alfalfa) 5·7
- Rice, white 5·6
- Maize, whole 5·5
- Cow's milk 5·3

Human milk 5·2
- Linseed 5·1
- Oats, rolled 4·6
- Egg, whole 4·5
- Sardine meal 4·4
- Peanut (groundnut) 4·4
- Wheat, whole 4·4
- Sesame seed 4·3
- Soya bean 4·1
- Wheat germ 3·8
- Yeast 3·6
- Cottonseed 3·2
- Sunflower seed 2·6
- Rye, whole —
- Peas, garden —

Tryptophan

Human milk 1·9
- Sesame seed 1·9
- Lucerne (alfalfa) 1·6
- Cow's milk 1·6
- Egg, whole 1·5
- Linseed 1·5
- Cottonseed 1·3
- Maize germ 1·3
- Rice, white 1·3
- Rye, whole 1·3
- Sardine meal 1·3
- Sunflower seed 1·3
- Yeast 1·3
- Oats, rolled 1·2
- Soya bean 1·2
- Wheat, whole 1·2
- Peanut (groundnut) 1·0
- Wheat germ 1·0
- Maize, whole 0·8
- Peas, garden 0·7

Phenylalanine
- Sesame seed 8·3
- Cottonseed 6·8
- Rice, white 6·7
- Oats, rolled 6·6
- Egg, whole 6·3
- Cow's milk 5·7
- Soya bean 5·7
- Wheat, whole 5·7

Human milk 5·6
- Linseed 5·6
- Rye, whole 5·6
- Maize germ 5·5
- Sunflower seed 5·4
- Peanut (groundnut) 5·4
- Maize, whole 5·0
- Peas, garden 4·8
- Sardine meal 4·5
- Lucerne (alfalfa) 4·5
- Wheat germ 4·2
- Yeast 4·1

* A dash indicates that Block and Mitchell give no value.

12

foods, arranged in ascending and descending order relative to the amounts in Mitchell, 1946–7)*

Cystine	Methionine	Threonine	Leucine	Isoleucine	Valine
	Egg, whole 4·1				
	Sardine meal 3·5				
	Cow's milk 3·4				
	Sunflower seed 3·4				
	Rice, white 3·4				
	Sesame seed 3·1				
	Maize, whole 3·1				
	Wheat, whole 2·5	Yeast 5·5			
	Oats, rolled 2·4	Linseed 5·1	Maize, whole 22·0		
	Lucerne (alfalfa) 2·3	Egg, whole 4·9	Maize germ 13·0	Cow's milk 8·5	
	Linseed 2·3	Maize germ 4·7	Cow's milk 11·3	Egg, whole 8·0	

Human milk 3·4	**Human milk 2·2**	**Human milk 4·6**	**Human milk 9·8**	**Human milk 7·5**	**Human milk 8·8**

Cystine	Methionine	Threonine	Leucine	Isoleucine	Valine
Egg, whole 2·4	Cottonseed 2·1	Cow's milk 4·5	Egg, whole 9·2	Sardine meal 6·0	Cow's milk 8·4
Cottonseed 2·0	Soya bean 2·0	Sardine meal 4·5	Rice, white 9·0	Yeast 5·9	Peanut (groundnut) 8·0
Soya bean 1·9	Yeast 1·9	Rice, white 4·1	Oats, rolled 8·3	Oats, rolled 5·6	Egg, whole 7·3
Linseed 1·9	Maize germ 1·6	Soya bean 4·0	Sesame seed 7·5	Rice, white 5·3	Linseed 7·0
Maize germ 1·8	Rye, whole 1·3	Sunflower seed 4·0	Yeast 7·4	Sunflower seed 5·2	Oats, rolled 6·3
Oats, rolled 1·8	Peanut (groundnut) 1·2	Peas, garden 3·9	Sardine meal 7·1	Sesame seed 4·8	Rice, white 6·3
Wheat, whole 1·8	Peas, garden 1·0	Wheat germ 3·8	Linseed 7·0	Soya bean 4·7	Maize germ 6·0
Peanut (groundnut) 1·6	Wheat germ –	Maize, whole 3·7	Peanut (groundnut) 7·0	Peas, garden 4·1	Sardine meal 5·8
Lucerne (alfalfa) 1·6		Sesame seed 3·6	Wheat, whole 6·8	Linseed 4·0	Sunflower seed 5·2
Maize, whole 1·5		Oats, rolled 3·5	Wheat germ 6·7	Maize, whole 4·0	Sesame seed 5·1
Rice, white 1·4		Wheat, whole 3·3	Soya bean 6·6	Maize germ 4·0	Rye, whole 5·0
Sesame seed 1·3		Lucerne (alfalfa) 3·3	Lucerne (alfalfa) 6·6	Rye, whole 4·0	Maize, whole 5·0
Sunflower seed 1·3		Cottonseed 3·0	Peas, garden 6·4	Lucerne (alfalfa) 3·6	Yeast 5·0
Peas, garden 1·2		Rye, whole 3·0	Sunflower seed 6·2	Wheat, whole 3·6	Wheat, whole 4·5
Sardine meal 1·2		Peanut (groundnut) 1·5	Rye, whole 6·2	Cottonseed 3·4	Lucerne (alfalfa) 4·4
Cow's milk 1·0			Cottonseed 5·0	Peanut (groundnut) 3·0	Soya bean 4·2
Yeast 1·0					Peas, garden 4·0
Wheat germ 0·8					Cottonseed 3·7
Rye, whole					Wheat germ

low compared with that of soya flour alone (65) or milk protein (74), but higher than that of white flour alone (41). The digestibility of the nitrogen was fairly high. Desikachar, De and Subrahmanyan (1948b) compared curd proteins from soya bean milk with protein of cow's milk as supplements to a poor south Indian rice diet whose proteins were from rice, dhal and gram. The supplemented diet provided about 65 g. of protein daily. All the subjects had large positive nitrogen balances which were about the same whichever the supplement.

Mitra, Verma and Ahmed (1948) copied the normal diet of the "poor rice eater" in which about 60 per cent of the protein came from parboiled rice and 30 per cent from pulses; the remaining 10 per cent was supplied by potatoes and vegetables. The protein of the diet had a biological value of 67, and when part of the rice was replaced by wheat, or mixtures of wheat and barley, wheat and maize, or wheat and millet, the biological value was always lower, 55, 60, 57 and 57, respectively. Mitra and Verma (1947) compared the supplementary effect of adding pulses or cow's milk to rice, and found that the biological value of the rice and milk mixture was about 9 per cent greater than of the rice and pulse mixture.

Perhaps the most extensive studies which have so far been made of the effects of supplementing the protein in human diets are those of Hegsted, Tsongas, Abbott and Stare (1946) and Hegsted, Kent, Tsongas and Stare (1947). The subjects were healthy young adults; in the basal diet the percentage of the protein derived from white bread made without the addition of milk solids was 50, from maize meal 7·6, from rice 4·4, from potatoes 13·3, from other vegetables (lettuce, carrots, onions and tomatoes) 16·3, and from fruit (orange juice, apples and peaches) 8·4, so that the protein was entirely of plant origin. One third of the protein was replaced by equivalent amounts from ground meat, wheat germ or commercial soya flour (made into biscuits), or white bread. The meat and wheat germ gave the best results; with them the biological value of the protein was high, the nitrogen balances were most nearly positive, and the actual amount of protein which had to be eaten to satisfy the body's daily needs was lower than with the other supplements. There were small differences in the amounts of nitrogen in the various diets, but these were not likely to have invalidated the results. The authors emphasized that their results applied to normal adults, and that the special demands of growth, reproduction and lactation were likely to be different. There is no reason to suppose, however, that if similar trials were made with infants, the general result would be different. It would have been of great interest if a milk supplement had been included in such carefully planned experiments, but the value of milk has been shown in human trials by many other workers.

There is a large body of evidence, which has been reviewed by Kon (1947–8) and by Widdowson (1947), showing that the addition of cow's milk to various diets causes improvements in the physique and clinical condition of children. Unfortunately for the present purpose, the amino-acid composition of the diet, with and without the addition of milk protein, was not estimated by direct analysis in any of the experiments. To do this would be of value as there is little doubt that some of the virtue which has been ascribed to milk protein really resides in its mineral or other constituents.

Gomez, Ramos, Bienvenu and Cravioto (1950) compared the value of milk and egg proteins with those of soya for feeding undernourished children. Fifty-eight children from 5 to 8 years old, in two groups, received about 50 g. protein daily, but one group had 22 g. from milk or eggs, and the other 20 g. from

soya bean, the rest of the protein being of vegetable origin. The diets were said to contain amino-acids in about equal proportions, but no details were given. The trial lasted 6 months, at the end of which no difference could be detected between the height and weight increase, the rate of haemoglobin formation, or the clinical condition, of the two groups. The diet containing the animal protein was slightly more effective in restoring the plasma proteins to normal levels.

The present author, working in Germany between the end of 1947 and the beginning of 1949, made some preliminary trials of barley, wheat and soya mixtures which had been recommended by Chick and Slack (1946) for infant feeding. Groups of children of various ages were given simple diets supplemented by cow's milk or by the cereal and soya mixtures. The cereals were malted and small quantities of dried skimmed cow's milk were added to some of the mixtures. A short account of the experiments has already been published (Dean, 1949). The full story of the trials forms the second part of this Report. It includes a discussion of the various difficulties encountered and the reasons for the uncertainty of some of the results. It was, however, concluded that cereal and soya mixtures could probably be prepared which would take the place of most of the milk in children's diets and might even replace it entirely. Comparable trials were made with animals, but it was recognized that much other essential work was left undone. The empirical methods which had to be used could not lead to more than a partial solution of the many problems involved. It was hoped to repeat the work, use being made of the experience gained, and to extend it by using other plant materials.

It is, therefore, evident that the use of vegetable proteins as supplements in human diets has given promising results, but that much more work is needed to provide a firm quantitative basis, particularly in respect of the individual amino-acids.

PART II: A DESCRIPTION OF SOME EXPERIMENTS IN THE USE OF PLANT PREPARATIONS

Introduction: The Animal Experiments of Chick and Slack with Soya Flour and Malted Cereals

AT the time of the liberation of Rome, in 1944, an acute food shortage arose because of the disruption of communications. There was very little for children to eat, and Dr. G. Caprino, of the Peroni Brewery, prepared an emergency food by malting certain cereals together. A few clinical trials were made in local hospitals, and the food appears to have served its purpose reasonably well. Few details are available but it was considered a valuable addition to the children's diets, especially when improved by addition of soya (Larsen, 1946; Ward-Perkins, 1950). The formula was brought to the notice of the United Nations Relief and Rehabilitation Administration, who requested Dr. Harriette Chick of the Lister Institute to investigate its nutritive value in biological experiments. Her report was published in 1946 (Chick and Slack, 1946).

She tested samples of two types of mixture, both of them in dry form. One contained 80 parts of an extract of malted barley, 10 parts of wheat flour of 80 per cent extraction, and 10 parts of skimmed milk powder; the other had soya flour in place of the skimmed milk. The wheat and soya flour had both been exposed for a short time to the action of malting enzymes. No details of the soya flour or of its previous treatment were supplied with the samples. It was a full fat flour.

The mixtures were given to weanling rats to provide about 10 per cent of protein, and were compared with a control diet which also contained 10 per cent of protein, all of it derived from cow's milk. The rats receiving the cereal and milk diet grew better than those that had the cereal and soya mixture, but not as well as the group having milk proteins only. The maximum rate of growth was, however, not attained because none of the diets provided more than 10 per cent of protein, and contained too little of the essential unsaturated fatty acids, since the rats developed scaly tail and skin lesions of the paws.

In another experiment with cereal and soya or cereal and milk mixtures, the proportions of protein derived from the various ingredients were altered by including 6 per cent more soya flour, or 10 per cent more dried skimmed milk, the amounts of protein thus provided being equal. The total protein in the diets was still about 10 per cent of the dry weight. Both additions gave the same result, and growth was equal to that of a control group whose dietary protein was derived entirely from milk. It was, therefore, concluded that "a combination of malt extract about 70 parts, wheat flour about 10 parts, and soya about 16 parts (on a solids basis) possesses a mixture of proteins whose growth-promoting value for young rats is about equal to that of the proteins of milk". Other conclusions reached were that the soya contained sufficient essential unsaturated fatty acids to prevent the onset of scaliness of the skin which had appeared with the diet containing protein only from cow's milk, and that the mixtures supplied the B vitamins in adequate amounts; the addition of yeast extract produced no extra benefit. In discussing the results, the authors pointed out that the amount of fat provided by their mixtures was only about one sixth of that provided by human milk, and stressed the need for clinical trials to decide whether human infants could thrive on such mixtures. They suggested that, for the trials, it might be advisable to include a small amount of skimmed milk in the diets.

There are a few details of Chick and Slack's work on which some comment is necessary. The protein in the soya flour used was found in other experiments (unpublished data) to have a supplementary value for the protein in white flour; this fact, and the satisfactory growth on the best of the cereal and soya diets, strongly suggest that the trypsin inhibitor (p. 19) had been wholly or partly destroyed by the malting enzymes or by some previous treatment. The former is a possible explanation in view of a report by McGinnis and Menzies (1946) that the inhibitor does not survive papain digestion. Destruction of the inhibitor by some other process in the preparation is equally possible because there seems no doubt, from the wide discrepancies between reports on the nutritive value of soya, that some commercial processes, especially those which involve heating, may destroy the inhibitor or at least render it innocuous.

It is possible that there were large differences in the amounts of minerals in the diets. Most of the minerals were supplied by the soya which, according to data quoted by Horvath (1938–9) contains one fifth of the calcium and one half of the phosphorus in the solids of human milk. It has consequently been usual when using soya for child feeding to redress the ratio of calcium to phosphorus by adding calcium (Mackay, 1940). This was not done by Chick and Slack; but their diets contained quantities, presumed adequate, of a salt mixture (McCollum No. 185), and their results do not suggest that addition of further calcium would have made any difference to the growth rates.

The Present Investigation

The experiments of Chick and Slack have been described in some detail because they were the starting point of the work which is to be presented. In 1947 a research unit of the Medical Research Council's workers was stationed at Wuppertal in north-west Germany, where it had been set up in the previous year to study questions of undernutrition. Friendly relations had been established with various hospitals and children's homes, and the opportunity arose to make some human trials of plant protein mixtures, similar to those found successful in the rat-feeding experiments. An account of the team's organization in Wuppertal has already been given (McCance and Widdowson, 1951b); it included, in addition to the various Institutions, a laboratory in the research section of the Elberfeld factory of the Bayer Corporation with adjacent animal houses for rats and dogs.

It was obviously desirable to study, if possible, children of all ages. Attention was concentrated on children of from 1 to 3 years, but children in the first year of life and others of from 3 to 5 and of from 7 to 11 years also took part in the trials. The trials were not all run simultaneously, and for simplicity the results have been presented in sections relating to the various age groups.

The Economic Background

The trials were held in the years 1947 and 1948 towards the end of the period of food shortages experienced in Germany after the war of 1939–45. Until a few months before the end of the war in Germany, the shortages were not severe, but from then onwards food distribution was uncertain and unequal. Although extra rations were provided for pregnant and nursing mothers, there was a small average reduction in the size of the children at birth, and in the amount of breast milk which the mothers could provide, for which the shortage of food was probably to a large extent responsible (Dean, 1951).
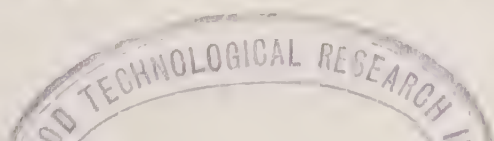
The effect on any individual mother or her child was impossible to assess, because the nutritional state of the family was really determined by the personal qualities of the mother and the other members of the family, and their ability to obtain food by barter or in the black market or from friends and relations in more fortunate localities. The economic recovery of the country was slow, but had certainly begun in 1947, and from then onwards continued steadily. The currency reform in 1948 had the effect of making more food available through the normal channels, but introduced the new factor of shortage of money which limited food purchases. Financial difficulties were said to bear very heavily on Institutions whose income was not fixed but derived, at least in part, from the individual contributions of parents or guardians. In one of the Wuppertal homes (the Augustinusstift) a large number of children was removed in the weeks following the currency reform, because even the very moderate charges of the home could no longer be paid. In the French Zone of Occupation, with which part of the present work was concerned because Ludwigshafen was situated in that Zone, economic recovery seemed to lag behind that in the other Zones.

The General Plan of the Experimental Work

The aim of the experiments was to assess the nutritive value for children of the combinations of proteins in various cereal and soya mixtures, similar to those used by Chick and Slack (1946). The mixtures were known to be innocuous to rats, but they had not been tried for feeding children. It was obviously wise to start with older children, and the first mixtures made were given for a month to children of from 3 to 5 years old before they were added to the diets of younger children.

Modifications of the mixtures for the children's use were always based on the results of animal experiments, which were of two types, growth tests and experiments to ascertain whether there was any likelihood of gastro-intestinal upset. The growth tests were made with weanling rats, which were usually given samples of the actual mixed diets served to the children. The experiments therefore differed from those of Chick and Slack, whose rats received diets in which the cereal and soya mixtures were the only source of protein. The distinction is important, because inclusion in a mixed diet subjected the cereal and soya mixtures to dilution and to the possibility of further supplementation. Some tests were made also with young dogs, because of their well known susceptibility to intestinal upset by diets containing a high proportion of sugar.

In each of the human trials, the groups of children were arranged to be as nearly as possible alike, and all the groups were given the same basic diet. For one group the basic diet was completed by addition of cow's milk and for the other groups by addition of the experimental mixtures.

Each child in the age groups up to 3 years was given as much food as it could eat, and the amounts were continually increased with increases in appetite. It is almost impossible to predict the food requirements of any individual child, and attempts to limit the amount of food taken would have frustrated one of the objects of the trials, which was to find the maximum amount of the cereal and soya mixtures which could be tolerated.

The children over 2 years old received each day in the form of drinks either a definite amount of one of the cereal and malt mixtures or an amount of milk having the same caloric value. Otherwise they had their ordinary diets.

As the chief purpose of the trials was to compare the value of various mixtures of proteins, it was important to make sure, as far as possible, that the results were not confused by shortage of any other dietary essential. In all the trials, vitamins A and D in the form of concentrates, and vitamin C as synthetic ascorbic acid or as orange juice were given to all the children. Unless it is stated to the contrary, each child received daily 2,000 I.U. vitamin A, 1,000 I.U. vitamin D and 50 mg. vitamin C. Calcium also was added to the diets where necessary to ensure that at least 1 g. was obtained daily.

The various biochemical investigations carried out included some analyses of the cereal and soya mixtures, and determinations of the activity of the trypsin inhibitor which is present in the soya bean and which had not been completely removed from the soya flour used in some of the mixtures. The rat experiments and some work on the inhibitor are described in Appendix E and D.

The Institutions in which the Trials were made

The trials were carried out at five places:

The Augustinusstift, Wuppertal-Elberfeld.
The Städtisches Waisenhaus, Duisburg.
The Goethe Schule, Ludwigshafen-am-Rhein.
The Gräfenau Schule, Ludwigshafen-am-Rhein.
The Landesfrauenklinik der Rheinprovinz, Wuppertal-Elberfeld.
The institutions are described in full for each age group.

Methods used in the Clinical Examinations

All the children under observation were examined clinically at the beginning and end of each of the trials.

The clinical examinations followed the same general pattern, but the details varied with the different age groups. The examinations were carried out by Dr. Andrew Barlow and the writer, working together, and, as they decided each point, a written record was made. The children were completely undressed and the heart and lungs were examined with the stethoscope. In the smallest children, special attention was paid to the general appearance, the condition of the skin, the quality of the subcutaneous tissue, and the muscle tone; the skull, ribs, wrists and ankles were examined for evidence of rickets, and the number of teeth was recorded. In the children between 1 and 2 years old, the neck and inguinal glands, tonsils, tongue and mucous membranes also were especially examined. In the older children the condition of the hair and the posture were noted with the other details.

When the examination of any child was complete, its condition was summed up and graded with one of the letters, A, B or C. The grading was made with much care, and was intended to express a clinical opinion which, although it took into account all the details, was not too much influenced by any one of them. This system was preferred to one based on numerical values allotted to the individual details, because it was not found possible to devise any such system that would yield gradings reliably reflecting the clinical judgment; clinical opinion is an entity not capable of mathematical definition. Such a method of clinical grading had the drawback that it was too inexact to be perfectly defined or reproduced, but no better system was known.

It was expected that if any disease was present which might complicate the results of the feeding trials it would be revealed by the clinical examinations, and that the examinations would enable the status and progress of the children to be described in clinical terms.

MEASUREMENTS OF WEIGHT AND HEIGHT

The children of up to 2 years old were weighed on a baby balance of the ordinary type, and the various balances were checked against one another and against standards at frequent intervals. The older children were weighed on pedestal balances which were standardized at the beginning and end of each trial.

The children of up to 2 years old were measured while they were supine, and the older children while standing upright with feet and knees together and legs straight. They were drawn up to their fullest height by gentle traction with the observer's hands on the sides of the head; the head was held so that the face was not tilted up or down.

HAEMOGLOBIN ESTIMATION

In one trial haemoglobin levels in the blood were measured in the children from 1 to 2 years old, and from 2 to 5 years old. The Haldane method was used. The blood was taken from the lobe of the ear, a fine sterile glass tube, made by drawing out a piece of ordinary glass tubing, being used to punch out a small disc of skin.

State of the Children at the Initial Examination

The size of the children at the beginning of the trials is shown in Table 13. At the Augustinusstift it was obvious that the children were rather small for their ages and that those in the group from 1 to 2 years old were the smallest. The group from 2 to 5 years old was considerably nearer to the standard size, and the children up to 1 year old were intermediate. At Duisburg the children who were of about the same ages as the oldest group at the Augustinusstift were slightly the smaller, and at Ludwigshafen, where the children were from 7 to 11 years old, the weights showed almost the greatest, and the heights the least, deviation from the standard.

TABLE 13

Percentage of standard height and weight for age of children at the beginning of Trial I (Wuppertal and Duisburg) and of the Ludwigshafen Trial

Group of children	Percentage of standard	
	Height	Weight
Augustinusstift		
6 to 12 months ..	94	88
1 to 2 years ..	91	81
2 to 5 years ..	93	92
Duisburg		
2 to 5 years ..	93	91
Ludwigshafen		
7 to 11 years ..	95	85

Children who were found to be diseased were excluded from the trials, so the clinical descriptions can be brief. Nearly all the Augustinusstift children were pale and rather flabby, but the typically bloated child with the appearance so often described by German doctors as due to excessive carbohydrate in the diet was not seen. The oldest children seemed to be normally lively, but the children from 1 to 2 years old were rather apathetic and inactive. The Duisburg children were less lively than normal children of their age, but the difference was probably not related to their state of nutrition; it was much more likely to have been the result of the rather stringent discipline to which they were subjected. The Ludwigshafen children, although on the whole pale and thin, were extremely eager and active.

The children at the Augustinusstift were well cared for and their skins were in good condition. Those at Duisburg, when first seen, had a considerable amount of minor sepsis which responded very quickly to simple treatment. This was somewhat to the surprise of the German doctor who attended the Home; he had expressed the opinion that such children had always had a considerable amount of sepsis, and that it could not be altered. The Ludwigshafen children, because they were living in their own homes, which must have differed a great deal in standards of cleanliness and affluence, were much more varied in appearance than any of the other groups. Most came from impoverished homes, and many of the homes were known to be bad. The children were usually fairly clean when they presented themselves for examination, but many had rough and dry skins which suggested infrequent washing. Hyperkeratosis, particularly of the arms, was fairly common, and many of the children had small septic lesions which were obviously rather chronic. The postures were, on the whole, poor, and there were many pot bellies which accentuated the apparent thinness of the legs. Almost every child had an enlarged thyroid gland; the isthmus was palpable in about 95 per cent, and the profile of the neck was altered by the gland in about 80 per cent. The Ludwigshafen children selected for the feeding scheme were, in general, in worse physical condition and smaller than the children of the same ages in the Duisburg Home who took part in the Unit's trials of different kinds of bread.

The Grouping of the Children and the Expression of the Results

In each of the trials in which different diets were compared, the different groups of children were arranged to be as nearly as possible identical. The same numbers of boys and girls, similar in age, clinical condition, weight and height for age, should ideally have been included in each group, but the ideal was not usually attainable, and the best approximation had to be made.

Experience proved that the simplest method of making the groups equal was to use slips of paper or card on which were written the name and age of each child, with code numbers denoting clinical condition and size for age. All the slips for children of one sex were sorted into order of age, and were then dealt one at a time to form the required number of groups. When all the slips were used, it was possible to see very quickly in what respects the groups were uneven, and how adjustments could best be made. The procedure was then repeated with the slips for the children of the other sex. Such an elaborate method was hardly necessary with very small groups, but unless it or a similar method had been used for the 625 Ludwigshafen children, the grouping would have been extremely difficult.

It was unfortunate, for easy analysis of the results, that the population of the Homes at Wuppertal and Duisburg was not stable. Children were constantly leaving and arriving, and the composition of the groups was affected unequally. It was therefore necessary to consider each child separately, instead of relying on the average gains for the groups. The actual gain in an experimental period was expressed as a proportion of the accepted standard gain of a child of the same sex and age, over the same length of time. The standard used throughout was derived from the tables of Meredith (1935), Boynton (1936) and O'Brien, Girshick and Hunt (1941).

An example may make the use of the method clear. In Trial I, Table 27, there is a girl, Annelie, who was 88 weeks old at the beginning of the trial and then weighed 10·35 kg. At the end of the trial which lasted 16 weeks she weighed 12·40 kg. and had, therefore, gained 2·05 kg. during the trial. The standard weight for a girl of 88 weeks was taken as 11·70 kg., and for one of 104 weeks as 12·30 kg.; the standard gain was, therefore, 0·60 kg. The result for the gain in weight of this child would, therefore, be expressed as:

$$\frac{\text{actual gain in weight, kg.}}{\text{standard gain in weight, kg.}} = \frac{2 \cdot 05}{0 \cdot 60} = 3 \cdot 42.$$

Percentage of the accepted body weight for age was used also, since it provides an easy and readily appreciated method of comparison with a standard. Thus the weight of the child, Annelie, was $\frac{10 \cdot 35}{11 \cdot 70} \times 100 = 88$ per cent of the standard at the beginning of the trial, and $\frac{12 \cdot 40}{12 \cdot 30} \times 100 = 101$ per cent of the standard at the end, a percentage gain of 13.

Both the methods of expression give some indication of progress towards, or away from, a standard size for age, but they are unsatisfactory in one way. They do not take into account the different potentialities of the children who start a feeding trial when near to their standard size, and of the others who are then far from that size. The child who has, for instance, 105 per cent of its standard weight at the beginning of a trial may thrive on a particular diet, but its weight at the end of the trial may still be the same percentage of the standard although it has all the time grown excellently. A child of normal height who has only 70 per cent of the standard weight at the beginning of the trial, and who ends the trial with the same percentage, will have grown poorly in comparison with the other child. Differences of this kind would not affect the results for whole feeding groups if the groups were so perfectly matched that each contained exactly similar children, but, in practice, and especially with such small numbers as were available in all the trials except that at Ludwigshafen, such matching was impossible.

The method of using groups of children, and giving each group a different diet, was not used for the newborn children at the Landesfrauenklinik. The tests with the newborn were only intended to give a preliminary indication of the possibility of using the cereal and soya mixtures in the feeding of such young children, and properly standardized trials were not practicable. The individual weight charts gave, however, a fairly clear indication of the children's progress.

The arrangement of the children in the various trials is shown in Table 14.

TABLE 14

Distribution of the children in groups according to age, the duration of the trials, and the feeding mixtures used

No. of trial	Age of group	Place of trial	Length of trial (weeks)	For results of trial see page:	Number of feeding groups in each trial and nature of supplement to basic diet*
I	6–12 months	Augustinusstift	12	76	
	1–2 years	Augustinusstift	16	83	3 { Fresh whole cow's milk *or* / Mixture A / Mixture B
	2–5 years	Augustinusstift	24	}103	
	2–5 years	Duisburg	24		
II	6–12 months	Augustinusstift	24	76	
	1–2 years	Augustinusstift	24	87	3 { Fresh whole cow's milk† *or* / Mixture B1 / Mixture B2†
	2–5 years	Augustinusstift	24	}104	
	2–5 years	Duisburg	22		
III	6–12 months	Augustinusstift	16	79	
	1–2 years	Augustinusstift	16	90	3 { Fresh whole cow's milk† *or* / Mixture C‡ / Mixture C2††
	2–5 years	Augustinusstift	16	}107	
	2–5 years	Duisburg	10		
	7–11 years	Ludwigshafen	13	112	4§ { Dried full-cream cow's milk *or* / Mixture C / Mixture C1 / Biscuits
	Newborn	Landesfrauenklinik	1–13	116	1 Mixtures D1 and D2

* For key to the composition of the feeding mixtures see p. 58.
† Infants aged from 6 to 12 months received only these two diets.
‡ Changed to Mixture D1 after 8 weeks at the Augustinusstift.
§ A fifth group of children not given any supplement was included in this trial.

The Cereal and Soya Mixtures used and their Manufacture

The mixtures of cereal and soya which were made for feeding the children were of four types, called A, B, C and D. Type A was made in England and the rest in Germany.

Type A. This was made from malted barley, and wheat and soya flours, the soya being steamed for a short time to remove the bitter material. The mixture of Type A resembled the mixture No. 7A of Chick and Slack (1946), and was made by the same manufacturer who made that mixture, except that the proportions of the ingredients were modified by reducing the amount of soya. The percentage of total protein in the mixture was only 9·3.

Calcium lactate and sodium chloride were added during manufacture.

Only one mixture of Type A was made.

Type B. This also was made from malted barley, wheat and soya flours, but the soya flour was steamed for longer than in Type A. The proportion of soya was higher and the finished product contained 17·6 per cent total protein.

As no calcium was added during manufacture, calcium carbonate was added later.

The mixture of Type B was used by itself and also in combination with 12·5 or 25 per cent of dried skimmed milk. The three Type B mixtures were named as follows:

    B—the plain mixture with no milk;

    B1—87½ parts of mixture B with 12½ parts skimmed milk powder;

    B2—75 parts of mixture B with 25 parts skimmed milk powder.

Type C. The same ingredients were used as for Type B, but the soya was steamed for a long period to remove the trypsin inhibitor as well as the bitter material. The total content of protein was about 18 per cent.

Calcium carbonate was added during manufacture.

Type C was used by itself and in combination with 10 per cent of dried skimmed milk. Type C was made also with fresh skimmed milk which was added during manufacture and dried with the other ingredients; the final product contained 10 per cent of skimmed milk solids.

The three mixtures were named as follows:

    C—the plain mixture with no milk;

    C1—90 parts of Mixture C with 10 parts skimmed milk powder;

    C2—the same as C, but with enough fresh skimmed milk added during manufacture to give 10 parts dried milk solids in the final product.

Type D. This was made from malted barley, maize instead of wheat flour, and soya flour. The soya was given a prolonged steaming as for Type C and fresh skimmed milk was incorporated as in Mixture C2. The percentage of total protein was about 17.

Calcium carbonate was added during manufacture.

Two mixtures of Type D were made, one on the laboratory scale and the other on the factory scale. They were called D1 and D2, respectively.

Note on nomenclature. The letters A, B and C without any suffix denote mixtures which were made without milk. When the suffixes 1 and 2 are used, they indicate that skimmed milk was added to the finished mixtures, or was incorporated during manufacture.

Manufacture of mixtures of Type A. To make Type A mixtures, 9·6 kg. National flour of 85 per cent extraction were taken up with about 50 litres of water in a steam-jacketed pan and stirred whilst being heated almost to boiling

in order to gelatinize the starch. After about 15 minutes enough cold water was added to reduce the temperature to 70° C., and 77·5 kg. malt extract (77 per cent solids) were stirred in. The temperature was maintained at 63° C. until tests showed that the whole of the starch had been converted to sugars; 9·6 kg. full-fat soya flour (20 per cent fat), 0·64 kg. sodium chloride and 2·7 kg. calcium lactate were added slowly and mixed. The whole was then passed through a sieve and concentrated at from 45° to 50° C. *in vacuo* to from 70 to 80 per cent solids. The resulting paste was spread out on trays and dried in a vacuum oven at from 45° to 50° C. The preliminary concentration and the final drying each occupied about 4 hours, and during that time there was undoubtedly some action of the malting enzymes on the wheat and soya flours.

Manufacture of mixtures of Type B. To make mixtures of Type B, 89 kg. barley malt flour and 11 kg. wheat flour of 70 per cent extraction were mixed with about 450 litres of water and the temperature was raised to 50° C., and maintained there for 45 minutes; it was then raised to 70° C. until the iodine reaction was negative. A portion was dried and analysed, with the following results:

					Percentage of dry weight
Glucose ..	..	..	..	..	6·7
Dextrin ..	..	..	..	..	23·7
Maltose ..	..	..	..	..	58·9
Protein ..	..	..	..	..	8·6
Ash, fibre	..	..	..	..	2·1

The soya beans (100 kg.) were steamed for about 50 minutes, dried, ground, and sieved. A fine powder was obtained amounting to 40 kg.; it contained 41·5 per cent of protein and 20·9 per cent of fat. The powder was suspended in water and added to a sufficient quantity of the malt suspension to provide 80 kg. malt solids, on a dry weight basis. The whole was concentrated to about 75 per cent solids in a vacuum pan, diluted to a consistency suitable for spray drying, put through a hair sieve, and spray dried.

One batch of Mixture B was used for Trial I and another for Trial II. They should have been identical, but may have differed in some unsuspected way (see p. 95-96).

Manufacture of mixtures of Type C. For Mixture C, a malt extract was made by taking barley malt flour and wheat flour and water as for Mixture B, filtering, and evaporating under reduced pressure until a syrup remained which had 78 per cent of solids. Finely ground soya flour, made as for Type B, was suspended in three times its own volume of water, and steam was passed through the suspension for 120 minutes. The manufacturer reported that after the heat treatment no trace of the trypsin inhibitor could be detected. The malt extract and the soya suspension were mixed and calcium carbonate was added. The mixture was diluted suitably with water and spray dried.

Mixture C2 was made in the same way as mixture C, except that before spray drying enough fresh, liquid, skimmed milk was added to give 10 per cent of milk solids in the dried product.

Manufacture of mixtures of Type D. Mixtures of Type D were prepared in the same way as Mixture C2, except that the malt extract was made from equal parts of barley flour and maize flour, the wheat flour of the other mixtures being omitted. Sucrose was added to the suspension before drying so that the final product contained 7·5 per cent of it in addition to the sugars provided by the malt extract.

Method of drying the mixtures of Types B, C and D. All the mixtures of Types B and C, and Mixture D2, were dried in a full-sized, commercial spray-drying tower, and it was intended that the temperature in the tower should not rise above 70° C. Unfortunately, however, control of the temperature was not perfect, and it was possible that temperatures up to 10° higher were sometimes reached. The hot-air current circulating in the tower was subject to variations, and considerable amounts of the powder adhered to the walls, from which they were periodically dislodged. The temperature in the small tower used for drying Mixture D1 could be accurately controlled.

Occurrence of overheating could be recognized because it caused a darkening in colour, which was, however, largely masked if fresh skimmed milk was incorporated.

PHYSICAL CHARACTERISTICS OF THE MIXTURES

The Type A mixture was a granular material, yellow-brown in colour, containing about 5 per cent of moisture. Its taste was very sweet and strongly malty.

Mixtures of Types B, C and D contained only about 0·5 per cent of water when they were taken from the drying tower, but took up another 3 or 4 per cent before they were tinned. All the mixtures were somewhat hygroscopic, but Mixture C2 was less so than Mixture C. It seemed that the incorporation of the fresh skimmed milk made drying easier and helped to produce a finer and smoother powder.

Mixture B was a yellowish-grey powder, fairly sweet in taste and definitely malty. It retained a little of the beany flavour of soya flour. The addition of skimmed milk powder in Mixtures B1 and B2 greatly improved the taste.

Mixtures of Types C and D were cream-coloured, and had a pleasant taste which was sweet and only slightly malty. No taste of soya could be detected. Mixture C, the only mixture of these types that was made without milk, was a little more malty in taste than the others.

All the powders could be reconstituted with water in much the same way as full-cream dried milk; Mixtures C2 and D1 were especially satisfactory in this respect.

ANALYSIS OF THE MIXTURES USED AS SUPPLEMENTS

The results of estimations of total nitrogen, fat, calcium, phosphorus, magnesium, iron and vitamin B_1 are shown in Table 15. The methods used are shown in a footnote to the Table.

The high figures for iron in most of the mixtures were almost certainly due to contamination from iron vessels during manufacture. Soya is, however, one of those vegetable materials which is comparatively rich in iron.

The percentage of protein was calculated from the total nitrogen by using the factors proposed by Jones (1931). The factors were for soya 5·71, cereals 5·83 and milk 6·38. For calculating the caloric value the factors 4·1, 9·3 and 3·75 were used for protein, fat and sugar. The values are given for 100 g. dry weight of the material; there was, however, always about 5 per cent moisture present, and the caloric value of the material as used was, therefore, about 400 Calories per 100 g. for all mixtures except A; for Mixture A it was only 375.

TABLE 15

Results of analyses of the cereal and soya, and of the cereal, soya and milk mixtures used in the child-feeding trials

Mixture	Trypsin inhibitor	Total N (g./100 g.)	Protein (g./100 g.)	Fat (g./100 g.)	Calcium (mg./100 g.)	Phosphorus (mg./100 g.)	Magnesium (mg./100 g.)	Iron (mg./100 g.)	Vitamin B_1 (µg./100 g.)	Calories (per 100 g. dry weight)
A	Not destroyed	1·61	9·3	2·6	631	345	86	1·8	0·46	392
B	Partly destroyed	2·95	17·6	7·5	211*	457	157	9·1	0·52	423
B1	Partly destroyed	3·28	19·2	6·6	342*	532	162	8·1	—	417
B2	Partly destroyed	3·60	21·4	5·7	747	607	146	6·9	—	415
C	Destroyed	2·93	17·5	7·3	556	489	—	—	—	421
C1	Destroyed	3·22	18·7	—	—	—	—	—	—	417
C2	Destroyed	3·20	18·6	6·5	778	506	—	—	—	417
D1	Destroyed	3·00	17·4	—	—	—	—	—	—	416
D2	Destroyed	2·92	17·0	6·3	750	485	—	—	—	416

* Calcium lactate 3 g. = 577 mg. Ca added to each 100 g. Mixture before use.
Methods of analysis used.
    Trypsin inhibitor. Method of Northrop, Kunitz and Herriott (1948).
    Total N. Micro-Kjeldahl technique with copper selenide as catalyst.
    Calcium, magnesium and fat. Methods described by McCance and Shipp (1933).
    Phosphorus. Method of Briggs (1922), as described by McCance and Widdowson (1943).
    Iron. Method of McCance, Widdowson and Shackleton (1936).
    Vitamin B_1. Thiochrome method, modified as described by Dean and Holman (1950).

Table 16 gives the percentage of total protein derived from the various ingredients of the mixtures. The diets No. 7 and No. 7A of Chick and Slack (1946) have been included for comparison. Mixture A had less soya, and Mixture B more soya, than diet No. 7A. There was no close counterpart to Chick and Slack's diet No. 7.

TABLE 16

Derivation of protein in the cereal and soya, and in the cereal, soya and milk, mixtures

Source of protein	Percentage of the total protein from each source in the:							
	diets used by Chick and Slack (1946)		mixtures used in the child feeding trials					
	No. 7	No. 7A	A	B and C	B1	B2	C1 and C2	D1 and D2
Barley ..	34	34	50	24	20	16	21	13
Wheat ..	11	10	9	4	3	3	3	—
Soya ..	30	56	41	72	60	48	62	61
Milk ..	25	—	—	—	17	33	14	14
Maize ..	—	—	—	—	—	—	—	12

TABLE 17

Amounts of 12 essential amino-acids in the cereal and soya, and in the cereal, soya and milk, mixtures
(All values are expressed in g. amino-acid per 16·0 g. N.)

Amino-acid	Diets used by Chick and Slack (1946)		Mixtures used in the child feeding trials*						Milk	
	No. 7	No. 7A	A	B and C	B1	B2	C1 and C2	D1 and D2	Cow's	Human
Arginine	5·1	5·9	5·4	6·2	5·9	5·6	5·9	6·1	4·3	4·3
Histidine	2·1	2·2	2·0	2·1	2·2	2·3	2·2	2·2	2·6	2·8
Lysine	5·3	4·9	4·6	5·3	5·6	6·0	5·6	5·4	7·5	7·2
Tyrosine	4·4	4·1	4·0	4·1	4·3	4·5	4·2	4·4	5·3	5·2
Tryptophan	1·3	1·2	1·2	1·2	1·3	1·3	1·3	1·2	1·6	1·9
Phenylalanine	5·6	5·7	5·6	5·7	5·7	5·7	5·7	5·6	5·7	5·6
Cystine	1·5	1·7	1·7	1·8	1·7	1·5	1·7	1·7	1·0	3·4
Methionine	1·8	1·8	1·6	1·8	2·1	2·3	2·0	2·2	3·4	2·2
Threonine	3·7	3·6	3·8	3·7	3·8	3·9	3·8	3·9	4·5	4·6
Leucine	7·3	6·5	6·5	6·5	7·3	8·1	7·2	9·1	11·3	9·8
Isoleucine	5·0	4·3	4·2	4·5	5·2	5·8	5·0	5·0	8·5	7·5
Valine	5·7	4·5	4·6	4·4	5·1	5·7	4·9	5·0	8·4	8·8
Percentage of total N accounted for by the 12 amino-acids	49	46	45	47	50	53	50	52	64	63

* Where the amount of an amino-acid is less than 75 per cent of the amount in human milk, the figures have been italicized.

PLATE 1. The Augustinusstift, Wuppertal

The approximate values of the various mixtures as sources of 12 essential amino-acids have been calculated and are set out in Table 17. The data in Block and Mitchell's Table 8 (1946–7) have been used where possible, but they did not include figures for barley. Inspection of the results of analyses made by Baumgarten, Mather and Stone (1946) showed that the amino-acid composition of barley was similar to that of rye, and Block and Mitchell's figures for rye were, therefore, used for barley. Deficiencies of more than 25 per cent of an amino-acid are indicated in Table 17. All the mixtures had less lysine, tryptophan, cystine, leucine, isoleucine and valine than human milk. Mixture A was especially short of lysine and had what appeared to be other large deficiencies, but the physiological importance of any of these shortages is uncertain. It is obvious that the inclusion of skimmed milk protein was, on theoretical grounds, an advantage. The high proportion of leucine in the mixtures of Type D was caused by the inclusion of maize in them. The proportion of the total N accounted for by the 12 amino-acids was always considerably less in the mixtures than in cow's milk and human milk.

Further discussion of the amino-acid content of the mixtures, in relation to the composition of the complete diets and the results achieved, will be found in a later section (p. 119).

ANALYSIS OF THE DIETS

The amounts of protein, fat and carbohydrate in the diets, and the caloric values of the various foods which were used with the cereal and soya mixtures, were calculated from the Tables of McCance and Widdowson (1946). Samples of the fresh whole milk used at the Augustinusstift were analysed for fat on several occasions by the Gerber method; the percentage of fat was always between 2·2 and 2·6.

Trials with Children of from 6 Months to 5 Years of Age in the Augustinusstift at Wuppertal-Elberfeld and in the Städtisches Waisenhaus at Duisburg

THE INSTITUTIONS

The Augustinusstift

This was a Roman Catholic Children's Home. It faced south on one of the many steep Wuppertal hillsides in the southern part of the town (Plate 1). It had suffered severely in one of the fire raids and 45 rooms had been burnt off the upper storeys; at the same time members of the staff had been killed and injured. The number of children had not decreased with the reduction in space available for them, so that there was much overcrowding, with the danger of cross-infection.

The wards were mostly small rooms, on the fifth, sixth and seventh floors of the Home, in which children of about the same age were kept together. Each ward was in the charge of a nun who was also a trained nurse, and she was assisted by student nurses who were spending two years in the Home to learn the care of children. There was a student nurse to about every four children. There was a ward in which children admitted to the Home were placed for an observation period usually of about six weeks, and other wards where sick children could be isolated and given special attention.

There was no doubt about the devotion and care given to the children, but the quality of the nursing varied from ward to ward, and was not high compared with that in a London teaching hospital. Diet and growth records were reasonably well kept. Perhaps the most serious criticism of the Home in addition to the overcrowding was in the very poor facilities for exercise and recreation in the open air. Loss of balconies which had been destroyed or had been enclosed to provide ordinary living room was partly the cause. Some other difficulties, such as shortages of linen and soap, and the very poor quality of the soap, appeared to give less trouble than might have been expected. The clothes of the children were always clean, and the wards themselves were constantly cleaned and polished, but the ventilation of them could have been improved.

The total number of children living in the Home at any one time was about 120; about 40 were from three to twelve months old, about 50 from one to two years old, and about 30 from three to four years old. They were in the Home for various reasons, and it was curious that very few of them were orphans in the strict meaning of that term. Many were the children of unmarried mothers; some could not remain at home simply because there was no accommodation there, some because the mother had married and the husband did not want her previously acquired child, and some because the parents had died or been killed in the war. Many of the children had been born in the Landesfrauenklinik and had come to the Augustinusstift with their mothers after the usual stay of from nine to ten days. Great difficulty was always experienced in persuading such mothers to breast-feed their children for any length of time. If anxiety did not adversely affect the supply of breast milk, the social circumstances of the mother usually made her want to be free from the responsibility. It will be seen, therefore, that although not many of the children were actually without parents, most of them were the victims of adverse circumstances. Their poor start in life may have had a bad effect on their physique.

A member of the nursing staff of the Unit was in charge of the work being done in the Home, and spent most of the day there. She had been trained in one of the London hospitals, and had had considerable experience of children. She was responsible for the preparation of the diets and their distribution, and for the collection and recording of the data relating to the feeding and health of the children.

In addition to the nuns and student nurses, there were at the Home a few nurses who had stayed there after completing their training. One of them, who, incidentally, had been severely injured in the fire raid which had caused so much other damage, became an assistant to the Unit, and one of the student nurses also was put at its disposal to help with serving the meals.

The German doctor in charge of the children lived in the building, but had a busy children's practice in the town which occupied most of his time. He visited the wards each morning at 8.0 a.m., and twice a week was accompanied on his rounds by the writer.

In general, the feeding of the children who were not ill, and all matters concerning the running of the trials, were supervised by the Unit. Children who became ill while taking part in the trials were reported at once to the German doctor whose ultimate responsibility was recognized and unquestioned, but any action to be taken, especially if it involved a change of diet, was decided by joint consultation. Throughout the trials this dual control of the children,

which might in other circumstances have been extremely awkward, worked with perfect smoothness.

Every child included in the trials was seen by the British nurse and doctor every day. The principle was established at the beginning of the trials and was adhered to rigidly. Every possible opportunity was taken of getting to know the children intimately as individuals. The members of the Unit appeared to enjoy the confidence of the German staff of the Home and were able to rely on a high degree of co-operation.

The diets on which the children were normally fed are described in relation to the supplements of milk and milk-substitutes given (p. 66); they were poor, and provided another reason why it could be expected that the children would be physically under-developed.

The children in the Augustinusstift were divided, for the purpose of the trials, into three age groups:

6 to 12 months,
1 to 2 years,
2 to 5 years.

The children aged up to 2 years seemed to have a very sedentary life, and even the oldest spent most of their lives in their cots, or at least rather strictly confined to their rooms. There were very few toys, and very little that might have added any interest to lives in which there were few opportunities for any activity except eating.

The children of from 2 to 5 years old had a greater degree of freedom. They were well dressed, and were cared for as individuals as well as the facilities of the Home allowed. They lived in two groups, divided by age, each group consisting of about fifteen children. The younger children ate, played and slept in one fairly large room, which was poorly ventilated, and which they did not leave very frequently. The older children lived a much more healthy life. They had dormitories as well as the room in which they lived during the day, and were taken for walks outside the Home whenever possible. It was easy to be critical of the apparent reluctance of the nurses to take their children into the open air, but it was a somewhat formidable undertaking to conduct large parties of children up and down the many staircases of the Home. The ascent from the level of the road to the seventh floor, where the children lived, involved climbing 117 stairs. There was a lift but its use by children was habitually avoided.

The Waisenhaus, Duisburg

The children in this orphanage were from 5 to 15 years old, and there were also about 30 younger children in the Home who occupied a day-room and two dormitories on the second floor, and they were included in the present trials.

The Duisburg Orphanage was a town institution, and had to shelter children who had been removed from unsuitable homes, or whose parents had disappeared or had been imprisoned. There were, of course, many other reasons for admission, but they all pointed to very unfavourable home conditions, and as might be expected the children were on the whole rather miserable and made a poor impression when seen together. They were badly dressed, and did not seem to be very happy. They were given very little individual attention, and no routine medical inspection. They were much inferior in appearance and mental development to the children of the same age at the Augustinusstift. They had, however, free access to the open air in the large playground of the orphanage.

PLAN OF THE FEEDING TRIALS WITH CHILDREN OF FROM 6 MONTHS TO 5 YEARS OLD AT THE AUGUSTINUSSTIFT AND AT THE WAISENHAUS, DUISBURG

Three successive trials, numbered I, II and III, were made with children of up to 5 years old at the Augustinusstift and the Waisenhaus. The children were divided into three groups by age, and each of the age groups was sub-divided into two or three smaller groups for feeding with different diets. Each of the divisions and sub-divisions was represented in each trial. The arrangement is explained in Table 14, where the nature of the diets is indicated and the duration of the trials is shown. Trial III was complicated by a change in the diet which was made after eight weeks because Mixture C2 and, to a less extent, Mixture C were found unsatisfactory.

The number of children in the Duisburg Home who stayed throughout any of the trials was very small. For this reason, and because the basic diet of these children resembled closely that of the corresponding children of from 2 to 5 years old at the Augustinusstift, the results for both Homes have been considered together.

The mathematical expression of the results has usually been confined to those children who completed the full course of each trial, but details are given of all children who showed signs of intolerance of the food, and of other children whose results could not be used because of illness. In a few exceptional cases, reference has been made to children who joined a trial after it had begun, or who left it for some reason unconnected with the food before it ended.

The results have been arranged so that all the children of one age group are dealt with together in one section. The value of the different supplements to each of the basic diets can thus be most easily compared. The results are expressed in the ways explained on p. 56, and usually, in addition to the whole record of progress throughout the trial, there are data for the ratio of actual to standard weight gain for shorter periods.

In reporting the results emphasis has been laid on measurements of weight rather than of height. This has been done partly because the weight measurements were certainly the more exact, particularly for the younger children, but also because it was found that increases of weight and height nearly always ran closely together; if a child gained well in weight it gained also in length. This result was probably made inevitable by the policy of always adding plenty of vitamin D and calcium to the diet. The additions were particularly necessary for children who were growing very rapidly; without them, rickets would almost certainly have developed.

The results of the three trials with each age group are summarized at the end of that section, and certain average values for the composition of the diets eaten are tabulated.

THE ORIGINAL DIETS OF THE CHILDREN, THE NATURE OF THE MODIFICATIONS INTRODUCED, AND THE METHODS OF KEEPING THE DIETARY RECORDS

Diets of Children of under 2 Years Old in the Augustinusstift

The Original Diets

The diets of the children of from 3 to 12 months old consisted largely of a semolina pudding known as "*Brei*", made by cooking ordinary coarse wheat

semolina with milk, much of which was skimmed. The original recipe was for 7 g. semolina and 5 g. sugar to each 100 g. milk, but with the increasing food shortage the sugar was sometimes omitted and the milk was watered. The consistency of the *Brei* was regulated with water. It was made thin for the early morning meal, thick at mid-day, when it was stirred into vegetables, and fairly thick in the afternoon.

Of the total quantity of fresh milk received by the Home, only a little was used in an unaltered state. Most of it was skimmed, and the cream was made into buttermilk and butter. The buttermilk was given always at the first sign of any gastro-intestinal upset, and also to healthy children once or twice a day. A few of the children had drinks of full milk as well.

The vegetables most commonly given were carrots, beetroot and spinach; they were finely sieved or made into a purée, and were served with butter. Occasionally stewed apples or prunes replaced the vegetables.

The whole diet was thus very simple. Vitamin supplements were not given regularly, but at the age of about 2 months each child was supposed to receive a large single dose (or "*Stoss*") of vitamin D. No ascorbic acid was given, but the amounts in the vegetables and perhaps in the milk were probably sufficient, as no signs of scurvy were seen.

The children of from 1 to 2 years old had almost the same diet as the younger children, including large amounts of the semolina *Brei*. Potato was added to the mid-day *Brei* four or five times a week, and on the other days green vegetables, swedes, turnips and carrots, some of them grown in the garden of the Home. The amounts of vegetable were large, some of the children receiving 200 or 300 g. in addition to from 100 to 200 g. of *Brei*. Melted butter was poured over the vegetables.

Bread was made in the Home from flour of a high rate of extraction, but the amounts eaten were usually very small, only a few of the children having more than from 30 to 40 g. a day. The bread was buttered. Some of the children had drinks of buttermilk or fresh milk, but the need for fluids was almost entirely met by the liquid part of the *Brei*.

There was no regular distribution of vitamins in a concentrated or synthetic form.

The Diets used in the Trials

The basic diet could certainly have been improved, but it was left undisturbed for the trials, in order that the usual practice of the Home should be upset as little as possible. Some measures were taken to ensure that it did not change from day to day. Thus extra supplies of semolina and sugar were provided so that the formula for the *Brei* could be constant. When fresh milk was used, it did not have to be diluted, because so much of the milk formerly used was replaced by the cereal and soya mixtures.

As explained on p. 52 there was in each of the trials a group of children receiving some cow's milk, and two other groups having diets in which the only difference was that one or other of the cereal and soya or cereal, soya and milk mixtures took the place of the cow's milk. The milk and the mixtures were used to make the semolina *Brei*, or were given as drinks. The *Brei* and drinks were made as follows:

Brei. The amounts of the various ingredients are shown in Table 18. Three kinds of *Brei*, thick, medium and thin, were made at different times of the day. The cow's milk *Brei* was made by adding the sugar to the milk, heating, adding

TABLE 18

Diets of children of up to 2 years old: amounts and calorie values of the ingredients for making 100 g. of the Brei used in Trials I, II and III

(The cereal and soya and the cereal, soya and milk Brei were completed by addition of water.)

No. of trial	Description of mixture*	Type of Brei	Cereal and soya mixture (g.)	Semolina (g.)	Fresh cow's milk (g.)	Dried skimmed milk (g.)	Sugar (g.)	Total Calories	Percentage of total Calories from: cereal and soya mixture	semolina	fresh cow's milk	dried skimmed milk	sugar
I	Mixture A	Thick	25·8	15·0	—	—	—	150	65	35	—	—	—
		Medium	19·3	11·2	—	—	—	112	65	35	—	—	—
		Thin	12·9	7·5	—	—	—	75	65	35	—	—	—
	Mixture B	Thick	20·25	12·5	—	—	—	125	65	35	—	—	—
		Medium	15·23	9·4	—	—	—	94	65	35	—	—	—
		Thin	10·12	6·25	—	—	—	62·5	65	35	—	—	—
II	Mixture B1	Thick	17·5	13·5	—	2·5	—	125	56	37	—	7	—
		Medium	13·13	10·0	—	1·87	—	94	55	38	—	7	—
		Thin	8·75	6·75	—	1·25	—	62·5	56	37	—	7	—
	Mixture B2	Thick	15·0	14·0	—	5·0	—	125	48	38	—	14	—
		Medium	11·25	10·5	—	3·75	—	94	48	39	—	13	—
		Thin	7·5	7·0	—	2·5	—	62·5	48	38	—	14	—
III	Mixture C	Thick	25·0	7·0	—	—	—	125	80	20	—	—	—
		Medium	17·5	7·0	—	—	—	94	73	27	—	—	—
		Thin	12·5	3·5	—	—	—	62·5	80	20	—	—	—
	Mixture C2	Thick	22·5	7·0	—	2·5	—	125	74	20	—	6	—
		Medium	15·75	7·0	—	1·75	—	94	67	27	—	6	—
		Thin	11·25	3·5	—	1·25	—	62·5	74	20	—	6	—
	Mixture D1	Thick	15·3	9·0	—	1·7	—	100	62·5	32	—	5·5	—
I, II and III	Cow's milk	Thick	—	12·0	82·0	—	6·0	110	—	37	41	—	22
		Medium	—	8·0	88·0	—	4·0	92·5	—	30	53	—	17

TABLE 19

Diets of children of up to 5 years old: amounts of the ingredients and calorie value of 100 g. of the drinks used in Trials I, II and III

(The cereal and soya and the cereal, soya and milk drinks were completed by addition of water.)

No. of trial	Nature of drink* and place of trial	Amounts of ingredients					Total Calories
		Cereal and soya mixture (g.)	Flour (g.)	Fresh cow's milk (g.)	Dried skimmed milk (g.)	Sugar (g.)	
I	Mixture A (Augustinusstift) ..	18·7	3·0	—	—	—	80
	Mixture A (Duisburg) ..	21·3	—	—	—	—	80
	Mixture B (Augustinusstift) ..	17·5	3·0	—	—	—	80
	Mixture B (Duisburg) ..	20·0	—	—	—	—	80
II	Mixture B1 (Augustinusstift) ..	17·5	3·0	—	2·5	—	90
	Mixture B1 (Duisburg) ..	17·5	—	—	2·5	—	80
	Mixture B2 (Augustinusstift) ..	15·0	3·0	—	5·0	—	90
	Mixture B2 (Duisburg) ..	15·0	—	—	5·0	—	80
III	Mixture C (Augustinusstift) ..	20·0	3·0	—	—	—	90
	Mixture C (Duisburg) ..	20·0	—	—	—	—	80
	Mixture C2 (Augustinusstift) ..	18·0	—	—	2·0	—	80
	Mixture C2 (Duisburg) ..	18·0	—	—	2·0	—	80
	Mixture D1 (Augustinusstift) ..	18·0	—	—	2·0	—	80
I, II and III	Cow's milk (Augustinusstift)† ..	—	3·0	97	—	—	63
	Cow's milk (Duisburg) ..	—	—	100	—	—	60
	Buttermilk (Augustinusstift) ..	—	—	94	—	6	56

* For key to designations of mixtures see p. 58.
† The youngest children had 95 g. milk with 5 g. sugar, and the Calorie value was 72 per 100 g.

the semolina and boiling for three minutes. For the cereal and soya *Brei*, a little more water was taken than the amount finally needed and the cereal and soya mixture was stirred in. It was then heated until it boiled, when the semolina was added and the whole was boiled for three minutes. Water was always lost during cooking, and the weight of the finished *Brei* had to be adjusted with

TABL

Specimens of diets eaten at the Augustinusstift by children of under 2 years (Co

No. of trial	Name of child	Age (weeks)	Diet		Time of feeding and amount in g.					Total amoun (g.)
			Designation of supplement*	Item	4 a.m.	8 a.m.	11 a.m.	4 p.m.	8 p.m.	
I	Gisela	43	Mixture B	Thick *Brei*	—	—	200	250	—	450
				Medium *Brei*	—	—	—	—	200	200
				Cereal-soya drink	—	200	—	—	—	200
				Buttermilk	180	—	—	—	—	180
				Vegetables	—	—	50	—	—	50
				Butter	—	—	7	—	—	7
										Total Per cen
I	Vera	60	Cow's milk	Thick *Brei*	—	—	200	250	—	450
				Medium *Brei*	—	200	—	—	—	200
				Buttermilk	180	—	—	—	180	360
				Vegetables	—	—	100	—	—	100
				Butter	—	—	4	—	—	4
										Total Per cent
I	Adelheid	96	Mixture B	Thick *Brei*	—	—	200	—	—	200
				Medium *Brei*	—	—	—	—	300	300
				Thin *Brei*	—	350	—	—	—	350
				Vegetables	—	—	200	—	—	200
				Butter	—	4	5·5	4	—	13·5
				Bread	—	40	—	40	—	80
										Total Per cen
III	Hubert	88	Cow's milk	Thick *Brei*	—	—	200	350	—	550
				Medium *Brei*	—	350	—	—	—	350
				Vegetables	—	—	200	—	—	200
				Butter	—	—	5·5	5	—	10·5
				Bread	—	—	—	50	—	50
										Total Per cen

* For key to nature of supplements see p. 58

water. The thickest *Brei* had to be eaten with a spoon, but the thinnest was like a thick soup and could be drunk when warm; when cold it set to a jelly.

Drinks. These were of several kinds and their composition is given in Table 19. The cereal and soya mixtures were stirred up with a little cold water, the required amount of hot water was added and the whole was heated until it

0

entrates of vitamins A and D, and ascorbic acid were given daily to each child.)

Calories				No. of Calories provided by:						
No. derived from:			Total	cereal and soya mixture	cow's milk	semolina or flour	vege-tables	butter	sugar	bread
protein	fat	carbo-hydrate								
79	92	355	526	180	99	195	—	—	32	—
30	37	137	204	60	44	84	—	—	16	—
28	24	108	160	140	—	20	—	—	28	—
23	14	63	100	—	72	—	—	—	—	—
—	—	15	15	—	—	—	15	—	—	—
—	56	—	56	—	—	—	—	56	—	—
160	223	678	1,061	380	215	299	15	56	96	
15	21	64	100	35	20	28	2	5	9	
65	112	318	495	—	203	184	—	—	108	—
26	52	107	185	—	97	56	—	—	32	—
46	28	126	200	—	144	—	—	—	56	—
—	—	14	14	—	—	—	14	—	—	—
—	32	—	32	—	—	—	—	32	—	—
137	224	565	926		444	240	14	32	196	
15	24	61	100		48	26	2	3	21	
41	32	177	250	162	—	88	—	—	—	—
47	36	199	282	183	—	99	—	—	—	—
35	28	155	218	142	—	76	—	—	—	—
—	—	138	138	—	—	—	138	—	—	—
—	108	—	108	—	—	—	—	108	—	—
25	10	165	200	—	—	—	—	—	—	200
148	214	834	1,196	487		263	138	108		200
12	18	70	100	41		22	12	9		16
79	137	390	606	—	248	226	—	—	132	—
46	91	186	323	—	169	98	—	—	56	—
—	—	111	111	—	—	—	111	—	—	—
—	84	—	84	—	—	—	—	84	—	—
15	6	104	125	—	—	—	—	—	—	125
140	318	791	1,249		417	324	111	84	188	125
11	25	64	100		33	26	9	7	15	10

boiled. The milk and the buttermilk were warmed with the sugar. The drinks were often given as bottle feeds, but the bottle with the cereal and soya mixtures had to be shaken occasionally as they tended to settle.

Specimens of the diets, with the caloric value of the items, and the distribution of the calories between protein, fat and carbohydrate, are given in Table 20.

Method of serving the diets. The bottle feeds for the small children were normally prepared on the fifth floor of the Home in a diet kitchen which was used also by the Unit for preparing the drinks and the mixtures. When one meal had been served, the dry ingredients for the next one were weighed out and stored in tins. On a serving table outside the kitchen door was a spring balance of the kind which can be set to take account of the weight of a standard receptacle. The receptacles were aluminium cans weighing 100 g., with tightly fitting lids. Each child had its own labelled can, and the cans were stacked, in a pre-arranged order, beside the balance. At a convenient height on the wall behind the cans were the schedules showing the amounts of food to be given to each child. The diet ready for serving was brought to the table. An assistant read the appropriate amount from the schedule and placed the first tin on the balance; it was filled, put on a tray, and closed with a lid. When a tray was filled, another assistant took it to the wards. The serving was thus exact and rapid, and the meal was still hot when it reached the children.

The oily solutions of vitamins A and D were usually added to the *Brei* and vegetable mixture served at mid-day. Vitamin C was usually given as orange juice, but if the children (or their nurses) objected to this method, tablets of ascorbic acid were crushed and given in a spoon.

When the serving was completed, the Unit's nurse went to the wards, saw some of the feeding and often helped with it, and was thus in a good position to assess the importance of any feeding difficulty. If the whole of the meal was not eaten, the tin was taken back to the serving table and the weight of the uneaten portion was determined and recorded. At the end of the day the amounts of food actually eaten were entered on each child's diet record, of which a specimen sheet is illustrated in Appendix A. The sheet was arranged so that at the end of the week the daily average of amounts eaten could be calculated simply and compared with the amounts offered. Spaces were provided also for calculating the number of calories and the percentages of protein, fat and carbohydrate consumed.

Each day the nurse and doctor of the Unit made a round of the wards together to discuss with the sister in charge the amounts of food offered to each child and such clinical matters as signs of intolerance of the cereal and soya mixtures. It was thus ensured that the children were always offered as much as they could eat, and that any gastro-intestinal or other illness was promptly detected.

Diets of Children of from 2 to 5 Years Old in the Augustinusstift and at Duisburg

The Original Diets

At the Augustinusstift, the early morning meal consisted of bread and butter with a drink of milk or "*Ersatz-Kaffee*". The mid-day meal was largely vegetables, chiefly potato, and once a week a little meat gravy. On Sundays there was a pudding, usually of cereals and milk, and a little jam. Occasionally on other days there was cooked fruit, usually apple. In the afternoon bread and butter was eaten again, with once or twice a week a small portion of

cheese, fish or sausage. At both meals the amount of bread was unlimited, so that no child should have been hungry.

Sweets and chocolate were a great rarity, and many of the children had never eaten them. A few children were visited sometimes by relations and friends who brought fruit, cake and biscuits, though it was officially forbidden to do so; such additions could never have been large, and they provided the only way by which the children could have obtained extra food.

At Duisburg the food of the children was equally plain. It was more monotonous in appearance and consistency, and was certainly less pleasantly served, than at the Augustinusstift. Breakfast consisted of "*Ersatz-Kaffee*", with bread and jam, and, very infrequently, butter. The mid-day meal was a vegetable soup, made by boiling whatever vegetables were available with wheat or other flour and some butter. Soya flour, a commercial product provided by the local Food Authority, was included occasionally. The afternoon meal was again soup, but made from cereals and sugar. The soups, especially that served at mid-day, were often of good flavour, but they seemed to an onlooker typically institutional in character with no time spared for consideration of individual tastes or appetites. As at the Augustinusstift, almost the only appearance of freshly cooked meat was as gravy added to the soup on Sundays. The last meal of the day, given just before bedtime, was usually of bread and jam with once a week cheese, sausage or fish instead of the jam.

It was said that a ration of whole milk was received by the Duisburg Home only for children of 4 years or under. The ration was very small, about 50 g. per head daily, and it was usually put into the cereal soup eaten in the afternoon.

Although the impression was originally gained that the basic diet at the Augustinusstift was better than that at Duisburg, a consideration of the ingredients showed very little difference and the total calorie intakes were probably adequate at both places (Tables 21 and 22), but there was much more that was pleasant about the preparation and serving of the meals at the

TABLE 21

Diets of children of from 2 to 5 years old at the Augustinusstift

Trial I

Typical recipes for main dish for mid-day meal

Constituent	Amount of constituent in 5 recipes for main dish (kg.)				
Oatflakes ..	5·0	—	—	4·0	4·0
Potatoes	—	14·0	14·0	—	—
Cabbage	—	—	4·0	—	—
Carrots	—	4·0	—	4·0	—
Tomato pulp ..	—	—	—	—	3·0
Apple pulp ..	2·0	—	—	—	—
Sugar	0·375	—	—	—	—
Butter	0·150	0·150	0·150	0·200	0·25
Cal./100 g. of main dish as served ..	96	57	54	77	71

The meals were cooked with water and portions of from 300 to 600 g. were served to each child.

TABLE 21 (*continued*)

Samples of complete diets

Meal	Diet item	Value of dietary items in complete diet on two separate days			
		Day 1		Day 2	
		Weight (g.)	Cal.	Weight (g.)	Cal.
Breakfast	Bread	40–80	100–200	40–80	100–200
	Butter	10	80	10	80
	Cereal and soya or milk drink	—	165	—	165
Mid-day meal	Main dish ..	300–600	250–450	300–600	250–450
	Apple	60	30	—	—
	Pancakes ..	—	—	60	120
Evening meal	Bread	40–80	100–200	40–80	100–200
	Butter	10	80	10	80
	Jam	5	15	—	—
	Cheese or sausage	—	—	20–30	60–100
	Cereal and soya or milk drink ..	—	165	—	165
		Total	985–1,385		1,120–1,560

Home-made cake and biscuits providing from 50 to 100 Cal. were sometimes served at the evening meal.

TABLE 22

Diets of children from 2 to 5 years old at the Waisenhaus, Duisburg

Trial I

Samples of soup recipes

Morning soup			
January 15, 1948		March 8, 1948	
Item	Weight (kg.)	Item	Weight (kg.)
Oatmeal	10·0	Barley	10·0
Carrots	10·0	Potatoes	10·0
Potatoes	10·0	Butter	0·75
Fat..	0·75		
Cal./litre	384	Cal./litre	330

TABLE 22 (*continued*)

Afternoon soup

January 30, 1948		March 5, 1948	
Item	Weight (kg.)	Item	Weight (kg.)
Oatmeal	7·0	Semolina	7·5
Sugar	2·0	Sugar	2·0
Soya flour.. ..	2·0		
Cal./litre	288	Cal./litre	340

Calories provided by various items in the diet

Item	Values for children from 4 to 5 years old		Values for children from 3 to 4 years old	
	Jan. 15, 1948 (Cal.)	March 8, 1948 (Cal.)	Jan. 30, 1948 (Cal.)	March 5, 1948 (Cal.)
Bread	526	588	496	492
Jam	20	74	24	24
Morning soup	288	247	127	135
Afternoon soup ..	150	170	72	85
Fish or cheese	42	—	50	84
Cereal and soya or milk drink	330	330	330	330
Total ..	1,356	1,409	1,099	1,150

Augustinusstift, and the children were not so obviously regimented at meals as those at Duisburg. The Augustinusstift children began eating with good appetite, but were inclined to flag later as normal children sometimes do; the Duisburg children showed no obvious pleasure in eating, but were never seen to leave any of their soup. They did occasionally leave bread at the last meal of the day.

At neither Home had the children regularly received any additional vitamins.

The Diets used in the Trials

The diets of the children at both Homes were left basically unchanged, but supplements in the form of drinks were given at the first and last meals of the day. One group of children had fresh whole milk, and two other groups had drinks made from the cereal and soya mixtures. Each portion of the drinks furnished 165 Calories, so that the daily addition was 330 Calories.

The drinks were made under the supervision of the Unit. At the Augustinusstift, the cereal and soya mixtures and the milk were prepared freshly for each meal by cooking them for a few minutes with 3 per cent of flour; they were served warm. At the Duisburg Home the drinks were served cold; they were made up once a day and kept in a cool place until required.

The amounts of the ingredients used for the drinks are shown in Table 19. The children were given capsules containing vitamins A and D, and ascorbic acid tablets. The caloric value of the diets was not calculated in detail as it was for the younger children, but the records were sufficiently complete for approximations to be made. Details of sample diets are given in Tables 21 and 22.

RESULTS OBTAINED WITH CHILDREN OF FROM 6 TO 12 MONTHS OLD IN THE AUGUSTINUSSTIFT

Trial I

Trial I began on December 22, 1947. There were three feeding groups in which the supplements given were the cereal and soya Mixture A (barley, wheat and soya flour, no skimmed milk powder, steamed for a short time), the cereal and soya Mixture B (barley, wheat and soya flour, no skimmed milk powder, stronger heating), and cow's milk. The mixtures were given in the form of drinks or *Brei*, but the *Brei* made with the mixtures was usually given with an equal amount of the *Brei* made with fresh cow's milk; the combination had a pleasant taste and was taken readily.

The mixtures were introduced gradually into the diets over a period of about six weeks, once a day at first, twice a day after a week or two, until they formed part of every meal. A careful watch was kept for signs of intolerance, but none was seen, and the children were given the mixed diet for another six weeks, the composition of the diets being recorded in full for this period. One child (Johannes, Diet B) was given more and more of the cereal and soya mixture *Brei* until all the cow's milk in his diet was replaced, without any sign of gastro-intestinal upset.

The results of the trial are given in Table 23. Data for the transition period in the first six weeks, and for the period of settled diets in the second six weeks, are provided. In the first period the gains were good, with little to choose between any of the groups. Several children were ill, four of them with pneumonia. Three of the four were in the group receiving Mixture B, and the fourth was in the milk group. Two of the three recovered excellently, but the third, who was known to be liable to chest troubles, made a slow recovery and subsequently had another severe attack of bronchitis. There was even more illness in the second period, and it affected particularly the group having cow's milk. Despite the setbacks, over the whole twelve weeks of the trial only four children out of twenty-one in all three groups failed to exceed the standard weight gain, and in each case illness was to blame.

The weight gains in the groups receiving the cereal and soya mixtures were usually greater than those in the group having milk. There was no illness which could be attributed to the cereal and soya mixtures and it was clear that, used in this way, they could replace a considerable amount of cow's milk. Their inclusion in the diets led to a slight increase in the average number of stools, but the increase was never great enough to cause alarm.

Trial II

In Trial II the change to the new diets was completed without ill effects within a week. The first full week began on April 3, 1948, and the trial lasted 24 weeks, until September 23, 1948.

Performance of children of from 6 to 12 months old in the Augustinusstift, expressed as change in percentage of standard body weight and as ratio of actual to standard body weight gain

Trial I

Supplement	Name	Sex	Age at beginning (weeks)	Percentage of standard weight			Ratio of actual to standard weight gain			Remarks
				at beginning	at end of 12th week	alteration	from 1st to 6th weeks	from 7th to 12th weeks	from 1st to 12th weeks	
Mixture A										
Malted barley, wheat and soya flour. No skimmed milk incorporated. Short steaming.	Maria	F	43	88	98	+10	3·26	1·02	2·28	Low starting weight due to attack of bronchitis. Throat infection in 11th week.
	Roland	M	40	63	75	+12	1·46	1·86	1·63	Low starting weight due to attack of bronchitis. Throat infection in 10th week.
	Monika	F	52	87	98	+11	2·82	0·01	1·62	
	Hubert	M	27	83	94	+11	1·49	1·72	1·58	Low starting weight due to ear infection.
	Norbert	M	41	88	91	+3	0·78	2·07	1·31	Grippe in 4th week.
	Hans Peter	M	46	80	83	+3	1·59	0·63	1·21	Ear infection in 10th week.
	Cosima	F	44	88	90	+2	2·17	0·01	1·16	Ear infection in 10th week.
	Alberich	M	58	78	80	+2	1·15	0·87	1·05	Appetite poor 11th to 12th weeks.
Mixture B										
Malted barley, wheat and soya flour. No skimmed milk incorporated. Longer steaming.	Gisela	F	33	80	93	+13	1·94	2·05	2·01	Bronchitis and pneumonia in first 6 weeks. Subsequently gained well.
	Eleanore	F	56	88	95	+7	0·94	2·59	1·68	Milk totally excluded from diet by 10th week.
	Johannes	M	52	95	100	+5	1·18	2·10	1·58	Loss of weight in 10th week for no apparent cause.
	Karl Heinz	M	44	95	98	+3	1·80	0·61	1·23	Throat infection in 5th week.
	Hedwig	F	29	94	94	0	0·84	1·33	1·04	Pneumonia in 2nd week, but made good recovery. Ear infection in 10th week.
	Klaus	M	54	85	84	−1	1·56	0·40	0·77	
	Barbara	F	43	82	77	−5	0·03	0·01	0·01	Pneumonia in 2nd week and bronchitis in 10th week.
Cow's milk	Vera	F	48	84	92	+8	2·59	0·80	1·82	Febrile illness (ear infection?), 10th to 12th weeks.
	Mathilde	F	36	78	84	+6	1·25	2·06	1·55	Low starting weight due to bronchitis.
	Hannelore	F	52	98	101	+3	2·37	0·01	1·30	Large child.
	Ursule	F	38	97	97	0	1·96	0·01	1·05	Throat infection in 11th week.
	Erika	F	36	93	93	0	1·11	0·04	0·81	Attacks of vomiting and diarrhoea in 7th to 10th weeks. No cause found.
	Peter	M	41	86	84	−2	0·02	1·15	0·57	Pneumonia in first weeks.

TABLE 24

Performance of children of from 6 to 12 months old in the Augustinusstift expressed as change in percentage of standard body weight and as ratio of actual to standard body weight gain

Trial II

Supplement	Name	Sex	Age at begining (weeks)	Percentage of standard weight			Ratio of actual to standard weight gain				Remarks
				at begin-ning	after 24 weeks	alter-ation	from 1st to 8th weeks	from 9th to 16th weeks	from 17th to 24th weeks	from 1st to 24th weeks	
Mixture B2											
Malted barley, wheat and soya flour. Skimmed milk, 25 per cent, incorporated. Longer heating,	Gudrun	F	35	72	83	+11	2·00	1·02	0·87	1·33	No illness, but appetite poor after 12 weeks.
	Gisela	F	47	92	98	+6	1·55	0·97	1·28	1·26	Diarrhoea of uncertain origin in 16th week.
	Kaspar	M	23	85	90	+5	1·25	1·45	0·88	1·22	Deterioration coincided with change of ward. Eczematous.
	Ferdinand	M	28	92	97	+5	1·33	1·34	0·90	1·20	Deterioration coincided with change of ward.
	Norbert	M	55	92	96	+4	0·97	1·21	1·29	1·17	*Grippe* in 4th week.
	Roland	M	54	69	73	+4	1·06	1·27	0·45	1·00	Feeding difficulty in 23rd week. Bronchitic.
	Cosima	F	58	91	90	−1	0·68	0·50	1·62	0·89	Appetite poor 6th to 12th weeks. Ear infection in 12th week.
Cow's milk	Sara	F	39	96	112	+16	2·11	1·95	1·66	1·91	In plaster for congenital dislocation of hip. No weight gained after 16th week although about 125 Cal. per kg. were taken consistently.
	Dietrich	M	52	74	88	+14	2·31	—	—	1·69	
	Barbara	F	57	81	89	+8	0·68	2·32	1·84	1·48	Appetite and weight loss in 6th week. No apparent cause.
	Michael	M	36	84	92	+8	2·00	0·90	0·86	1·28	No cause found for deterioration.
	Hedwig	F	43	96	102	+6	1·31	1·30	1·04	1·21	Liable to gastro-intestinal upsets uncertain origin.
	Benedikt	M	31	93	97	+4	2·50	negative	0·89	1·14	
	Mathilde	F	50	83	87	+4	1·45	0·90	0·89	1·10	Appetite capricious. Liable to gastro-intestinal upsets of uncertain origin.
	Hans Peter	M	60	85	86	+1	1·31	1·10	0·02	0·91	Appetite good (110 Cal. per kg. eaten). No illness. No cause found for failure to gain weight in 17th to 24th weeks.

There were only two feeding groups. One had Mixture B2 (75 parts of Mixture B as used in Trial I with 25 parts of dried skimmed milk) and the other had the cow's milk diet. The plan of giving *Brei* made from the cereal and soya mixture together with cow's milk *Brei* was not followed in Trial II. The effect was to reduce the amount of cow's milk in the diet of the group having Mixture B2. The *Brei* made with Mixture B2 was well liked.

The results are given in Table 24. Those of the group receiving the cow's milk were rather more consistently good, but illness played an important part in reducing weight gains. In such a long trial it was to be expected that children would be moved from one ward to another; two of them, Kaspar and Ferdinand, having Mixture B2, suffered notably from such a change. There were a few failures for which no cause could be found; several of them were among children who were in the group having cow's milk.

None of the illness appeared to be caused by the cereal and soya mixture. A few of the children having Mixture B2 had a temporary loss of appetite, and one of them (Roland) spoilt his otherwise good record in this way. Another child (Gisela) had an attack of diarrhoea, but it was almost certainly of infective origin. Loss of appetite affected also various children having the milk supplement. Recovery from infection was apparently as rapid and complete in the one group as in the other.

At the end of the trial, the clinical condition of the children was on the whole very good, and there was no difference between the groups.

One reason for satisfaction with Trial II was that the percentage of the cereal and soya mixture included in the diets had been raised (see Table 26), without causing any gastro-intestinal disturbance.

Trial III

Trial III, like Trial II, had only two feeding groups; it was intended that one should receive Mixture C2 (containing soya from which the trypsin inhibitor had been removed, and 10 per cent solids from fresh skimmed milk incorporated during manufacture), whilst the other should receive the usual milk diet.

The sample material supplied appeared to be of such excellent quality, and was so free from any tendency to cause diarrhoea when given to dogs, that it was decided to alter the *Brei* recipes so that the amount of semolina used was less. The alteration had the effect of considerably increasing the proportion of the cereal and soya mixture in the complete diet (see Table 26). It had contributed 42 per cent of the total calories in Trial II, and the percentage now rose to 59 per cent. When the alteration was made, it was not appreciated that Mixture C2 as delivered in bulk was greatly inferior to the preliminary sample, probably because of some change in the carbohydrate which caused loose stools (see pp. 125, 136).

The trial lasted sixteen weeks from September 25, 1948 to January 15, 1949. The first four weeks were occupied in accustoming the children to the new diets, but there was a decided tendency for Mixture C2 to cause loose stools, which, although they did not seem to upset the children in any other way, were associated with poor weight gains. In the circumstances, the diet was changed at the end of the eighth week, and the children were given instead the experimental Mixture D1, for which the malt extract was made from equal quantities of barley and maize, and sucrose was added. The soya flour was subjected to prolonged heating and 10 per cent of skimmed milk solids were included. The composition of the *Brei* was altered by the inclusion of more

semolina than had been used in the diet with Mixture C2. Only one kind of *Brei* was made with a Calorie value of 100 per 100 g. There were fewer complaints of loose stools, and the weight gains showed an improvement, which was confirmed by the behaviour of a few other children who were added to the group for the last four weeks of the trial. The results are given in Table 25;

TABLE 25

Performance of children of from 6 to 12 months old in the Augustinusstift, expressed as change in percentage of standard body weight and as ratio of actual to standard body weight gain

Trial III

Supplement	Name	Sex	Age at beginning (weeks)	Percentage of standard weight			Ratio of actual to standard weight gain	Remarks
				at beginning	after 8 weeks	alteration		
				First 8 weeks				
Mixture C2	Bruno ..	M	42	93	96	+3	1·38	
Malted barley, wheat	Agnes ..	F	37	99	101	+2	1·30	
and soya flour; 10	Cristel ..	F	56	67	69	+2	0·82	Some loose stools.
per cent dried skim-	Rosemarie	F	43	86	84	−2	0·55	Always difficult to feed. Appeti
med milk incorpor-								poor. Stools loose.
ated. Trypsin inhibi-	Gudrun ..	F	60	82	80	−2	0·44	Appetite poor. Stools loose.
tor removed by pro-	Dietrich ..	M	77	88	86	−2	0·01	Stools constantly loose. Former
longed heating.								in plaster (see Trial II, Table 2
								and did not gain weight sat
								factorily when taken out.
Milk	Kaspar ..	M	48	91	102	+11	2·75	
	Roland ..	M	79	73	79	+6	2·24	Temporarily free from bronchit
	Nikolaus	M	55	87	96	+9	2·18	Large appetite; 120 Cal. per k
								eaten.
	Karl ..	M	44	67	76	+9	2·00	
	Ferdinand	M	53	94	100	+6	1·91	Low starting weight due to rece
								change of ward.
	Herbert ..	M	44	84	87	+3	1·25	
				Second 8 weeks				
Mixture D1	Rosemarie	F	51	84	86	+2	1·49	Appetite much improved whe
As Mixture C2, but								diet changed.
maize instead of	Cristel ..	F	64	69	71	+2	1·15	
wheat flour.	Agnes ..	F	45	101	100	−1	0·86	Large child. Throat infection i
								16th week.
	Gudrun ..	F	68	80	80	0	0·70	Appetite improved but throa
								infection in 12th and 16th wee
	Dietrich ..	M	85	86	85	−1	0·56	Occasional loose stools.
	Bruno ..	M	50	96	91	−5	0·20	Appetite poor. Stools loo
								Changed to milk diet in 15
								week.
Milk	Karl ..	M	52	76	81	+5	1·65	Throat infection in 14th week.
	Kaspar ..	M	56	102	104	+2	1·25	Large child. Eczema of face
								10th week. Treated by int
								ducing Mixture D1 *Brei* into
								feeds. Result good.
	Herbert ..	M	52	87	88	+1	1·03	
	Ferdinand	M	61	100	97	−3	0·36	*Grippe* in 14th week. Large chi
	Roland ..	M	87	79	76	−3	negative	Ear infection in 9th week. Br
								chitic.
				12th to 16th weeks				
Mixture D1	Dieter ..	M	23	86	94	+8	3·10	
As Mixture C2 but	Grete ..	F	38	112	114	+2	1·74	
maize instead of	Marlise ..	F	23	79	80	+1	1·28	
wheat flour.	Stephanie	F	26	86	84	−2	0·76	Some loose stools.

they show that there was little difference in the weight gains of the children given Mixture D1 and of those given the milk diet. Clinically there was no difference between the two groups.

Summary of Trials I, II and III with Children of from 6 to 12 Months Old

A summary of the weight gains, given in graphical form in Fig. 1, shows
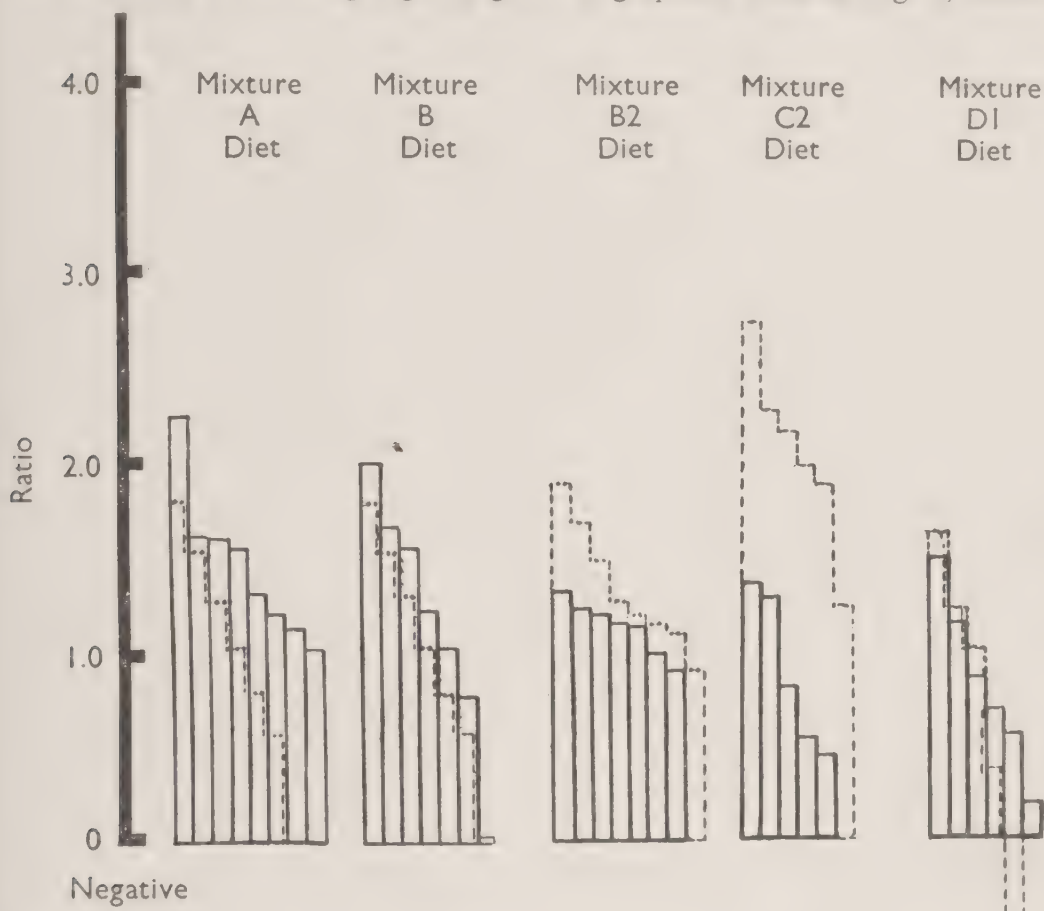
Fig. 1.

Ratios of actual to standard weight gains of children of from 6 to 12 months old given the cereal and soya supplements. The dotted lines indicate the ratios for the children in the groups given the milk supplements.

MIXTURE A.   Malted barley, wheat and soya flours. No dried skimmed milk. Short heating.
MIXTURE B.   Same as Mixture A. Longer steaming.
MIXTURE B2.   Same as Mixture B with 25 per cent of skimmed milk powder.
MIXTURE C2.   Same as Mixture B2 but heated long enough to remove trypsin inhibitor.
MIXTURE D2.   Same as Mixture C2 with maize instead of wheat flour.

that four out of the five cereal and soya mixtures gave good results; the fifth, Mixture C2, was the only one which did not produce growth approximately equal to that in the contemporary group having milk. The explanation was almost certainly to be found in the tendency of the mixture to cause gastro-intestinal upset.

The trials showed the difficulties of assessing the value of any diet in circumstances where illness, for which the diets could not always be held responsible, was able to play such a large part. In spite of the uncertainty thus introduced

it was, however, clear that unless the manufacture was seriously at fault, as it probably was in the preparation of Mixture C2, a combination of cereal and soya mixture with a small amount of milk had a nutritive value which was hardly inferior to that of a diet containing much more milk.

The composition of the diets is shown in Table 26. The highly successful diets containing Mixtures A and B, used in Trial I, each derived 29 per cent of their total calories as protein from fresh whole milk. The diet with Mixture B2

TABLE 26

Children of from 6 to 12 months old in the Augustinusstift: average values for the diets eaten in Trials I, II and III and the distribution of calories among the various items of the diets

Sources of calories	Trial I		Trial II	Trial III		Trials I, II, III
	Mixture A diet	Mixture B diet	Mixture B2 diet	Mixture C2 diet	Mixture D1 diet	Cow's milk diet
Cal. per kg. body weight from:						
Protein	13	15	20	19	18	14
Fat	16	21	14	19	17	25
Carbohydrate	71	65	77	72	72	63
Total ..	100	101	111	110	107	102
Percentage of total cal. from:						
Protein	12	15	18	18	16	14
Fat	14	21	13	17	16	24
Carbohydrate	74	64	69	65	68	62
Percentage of total cal. from:						
Cow's milk	17	22	17	13	12	44
Cereal and soya mixture	36	33	42	59	50	0
Semolina..	31	28	30	17	28	30
Vegetables	3	4	3	4	2	2
Butter	4	5	5	4	5	4
Sugar	9	8	3	3	3	20
Percentage of total cal. as protein from:						
Cow's milk	29	29	39	31	25	63
Cereal and soya mixture	33	40	44	61	56	0
Semolina..	38	31	17	8	19	37
Number of diets averaged	8	6	11	5	10	19

used in Trial II was similar as far as the percentage of the total calories coming from the different ingredients was concerned, but the percentage of the protein calories coming from milk was 39; the milk was skimmed milk, dried. The results in Trial II were not superior to those in Trial I, and it seemed that no advantage had been obtained by raising the proportion of milk protein. In Trial III the milk was reduced in total amount, and was fresh skimmed milk, which was dried with the cereal and soya mixture during the manufacturing process. It provided from 25 to 31 per cent of the total protein calories.

The amount of cereal and soya mixture in the diets was lowest in Trial I, greater in Trial II, and greatest in Trial III. The degree of success achieved was not correlated with this increase. The different kinds of milk used, and differences in the manufacture of the mixtures, were more likely to have been responsible for the variations in the results. It was disappointing that the first preparation, Mixture C2, in which complete removal of the trypsin inhibitor was achieved, should have been associated with increase in digestive troubles, but it was at least made clear that the inhibitor itself was not the cause of the upsets.

Details of the diet with cow's milk, which remained unchanged throughout the trials, are included in Table 26 for comparison. The diet had two sources of protein, cow's milk and semolina. The former supplied about two thirds of the total protein; none of the other diets contained nearly as much.

RESULTS OBTAINED WITH CHILDREN OF FROM 1 TO 2 YEARS OLD
IN THE AUGUSTINUSSTIFT

Trial I

There were three feeding groups in Trial I. Two received the cereal and soya Mixtures A and B, and the third cow's milk. Mixtures A and B contained barley, wheat and soya flour and no skimmed milk. Mixture B was heated for longer than Mixture A. The children having Mixtures A and B did not have any cow's milk at all during the course of the trial, except where the contrary is especially stated. The new diets were given in increasing amounts over the course of about four days, and the first week of the trial began on November 29, 1947. The last week ended on March 19, 1948, sixteen weeks later.

The results are given in Table 27. It is clear that Mixture A was a failure and Mixture B a success when used in the conditions of this trial. The chief reason for the failure of Mixture A was that it was disliked by the children and caused loose stools; as might be expected, the weight gains were poor. Only one child (Simson) gained weight well, and he became excessively fat and flabby. At the end of the trial his clinical condition was adjudged unsatisfactory because of the excessive fat. He graduated to the more varied diet of the older children soon after the end of the trial, and became more normal in appearance during the next fifteen months. During that time, however, he gained very little more weight. His progress is shown in Fig. 2. Two children (Ulrika and Franz) appeared to be unable to tolerate even small amounts of Mixture A and had to be given a milk diet; two others (Harry and Kunigunde) progressed fairly well on a diet in which Mixture A Brei was given with an equal amount of cow's milk Brei, and one child (Hans Walther), whose stools were bad when he was given the Mixture A diet, was transferred to the Mixture B group and given three quarters Mixture B Brei and one quarter cow's milk Brei, with good effect. Most of the few children who could safely be kept on the Mixture A diet had attacks of diarrhoea, which were certainly attributable to the mixture. The opinion was confirmed in many tests by the prompt appearance of gastro-intestinal upsets when the mixture was added to milk diets which had been proved innocuous.

The results of feeding with the Mixture B diet were fortunately quite different. The weight gains were good, and close to those of the children who had the milk diet. There were a few transient attacks of diarrhoea but they were almost always associated with an infection, and the mixture was apparently not

TABLE 27

Performance of children of from 1 to 2 years old in the Augustinusstift, expressed as change in percentage of standard body weight and as ratio of actual to standard body weight gain

Trial I

Supplement	Name	Sex	Age at beginning (weeks)	Percentage of standard weight			Ratio of actual to standard weight gain			Remarks
				at beginning	after 16 weeks	alteration	from 1st to 8th weeks	from 9th to 16th weeks	from 1st to 16th weeks	
Mixture A	Simson	M	103	69	79	+10	0·50	5·00	2·80	No gain for 5 weeks. *Grippe* in 5th week.
Malted barley, wheat and soya flour. No skimmed milk incorporated. Short heating.	Hans Günther	M	86	73	76	+3	negative	2·81	1·32	*Grippe* and loose stools in 5th and 7th weeks.
	Ingrid	F	77	96	96	0	negative	negative	1·08	Stools bad at first, but improved later. Bronchitis in 5th week, ear infection in 9th week.
	Udo	M	74	72	72	0	1·00	3·00	0·65	
	Wolfgang	M	65	81	78	−3	0·01	0·83	0·42	Stools bad throughout.
	Annemarie	F	92	76	71	−5	negative	negative	negative	Bronchitis in 4th week. Stools bad.
	Heinz	M	64	104	95	−9	0·55	negative	negative	Throat infection in 4th and 17th weeks. Stools bad.
	Susanna	F	99	98			0·50			No gain for 5 weeks. *Grippe* in 5th week. Left the Home in the 14th week.
	Hans Walther	M	80	73			negative	3·30		Stools bad on Mixture A diet. Changed to Mixture B(⅔) and cow's milk (⅓), and grew well (see p. 83).
	Harry	M	59	82			negative	0·80		Stools bad, and no weight gained until diet changed to half Mixture A *Brei* and half cow's milk *Brei*. Stools and weight then improved.
	Kunigunde	F	74	85			negative	5·00		
	Ulrika	F	65	80			negative			Could not tolerate Mixture A. Stools very bad. Changed to milk diet.
	Franz	M	75	73			negative			

Mixture	Name	Sex								Remarks
Mixture B — Malted barley, wheat, and soya flour. No skimmed milk incorporated. Longer heating.	Annelie	F	88	88	101	+13	2·00	4·27	3·42	Grippe in 4th week; good recovery.
	Diethard	M	87	72	84	+12	2·03	3·38	2·68	
	Detlef	M	90	78	89	+11	1·38	3·62	2·50	Grippe and ear infection in 15th week.
	Eva	F	66	68	78	+10	3·50	1·01	2·32	Ear infection in 15th week.
	Isette	F	66	72	82	+10	2·51	1·72	2·12	Ear infection in 5th and 8th weeks.
	Ruprecht	M	80	90	96	+6	negative	5·08	1·75	Throat infection in 14th week.
	Gerda	F	94	76	79	+3	2·16	0·59	1·43	Throat infection with diarrhoea in 3rd week. Recurrence of throat infection in 5th and 14th weeks.
	Liselotte	F	62	93	98	+5	0·94	1·88	1·38	
	Hans Josef	M	77	72	75	+3	1·16	1·20	1·19	Grippe in 4th week. Throat infection in 14th week.
	Adelheid	F	90	105	105	0	2·90	negative	1·08	Gained despite throat infection and bronchitis in 3rd and 5th weeks. Over-weight child.
	Heinz Peter	M	92	84	84	0	0·83	0·80	0·93	Bronchitis in 3rd week. Ear infection in 7th and 15th weeks.
	Bernhard	M	65	86	86	0	1·51	0·01	0·78	Vaccination reaction and bronchitis in 3rd week. Bronchitis again, with loose stools, in 12th week.
	Renate	F	61	96			negative			Bronchitis in 4th week. Subsequently gained well, but left in 12th week.
	Paul Josef	M	90	87			1·84			Throat infection in 2nd week. Left in 13th week when gaining well.
	Manfred	M	91	97			0·25			Throat infection in 2nd week and again with Grippe in 5th to 7th weeks. Left in 14th week when gaining satisfactorily.
	Wolfram	M	67	72						Stools rather loose on full Mixture B diet, but greatly improved when ¾ Mixture B and ¼ cow's milk were given.
Cow's milk	Laurenz	M	89	60	79	+19	4·00	3·48	3·75	Grippe in 6th week.
	Gordona	F	91	85	96	+11	2·84	3·62	3·21	Ear infection in 14th week.
	Margret	F	83	91	102	+11	3·50	2·52	2·80	Bronchitis in 4th week.
	Hans	M	75	93	103	+10	1·71	3·76	2·75	Throat infection in 15th week.
	Emilie	F	98	93	101	+8	3·22	negative	2·54	Pneumonia in 6th week; good recovery.
	Brigitte	F	57	81	93	+12	0·95	3·84	2·19	Grippe in 3rd week.
	Horst	M	73	80	89	+9	1·13	2·82	1·93	Grippe in 4th week.
	Petrus	M	87	70	77	+7	2·22	1·46	1·86	Throat infection in 8th week.
	Sophie	F	85	83	86	+3	1·13	2·13	1·66	Ear infection in 4th and 15th weeks.
	Günther	M	69	98	101	+3	0·98	1·73	1·34	To 2 to 5 year group in 12th week (see Table 35).
	Lili	F	57	81	83	+2	0·76	1·63	1·12	To 2 to 5 year group in 12th week (see Table 35).
	Roswitha	F	73	77	78	+1	1·00	0·96	0·97	
	Parsival	M	105	91			1·11			
	Jurgen	M	95	82			4·47			

Fig. 2.

SIMSON: *Weight curve.*

···●···●···, standard weight
—×—×—, actual weight

In the 14 weeks before Trial I began the child gained no weight. He was given Mixture A but did not gain for another 4 weeks; then after a mild attack of *Grippe*, when his weight became only 67 per cent of the standard, he grew very fast and by the end of the trial was 79 per cent of the standard weight. To achieve this he ate about 140 Cal. per kg. daily.

In Trial II he was given Mixture B2 diet for a short time but then joined the group of children aged from 2 to 5 years in Trial III. He was not actually ill but gained no more weight for 20 weeks.

At the end of Trial I he was found on clinical examination to be excessively fat and it was believed that the Mixture A diet had been responsible.

responsible. Only one child (Wolfram) showed signs of intolerance; he had loose stools when given the full Mixture B diet, but improved greatly when one quarter of his *Brei* was replaced by milk *Brei* (see Fig. 4 (*d*), p. 98).

The complicating effects of illness from causes other than the diets are clear in Table 27. In assessing the results it must be borne in mind that the diet containing Mixture B was one which, by ordinary standards applicable in most European countries or in the United States, would be considered inadequate or at least ill-balanced. There was no cow's milk or other animal protein in the diet (see Table 32), and yet it proved to be very little inferior to the control diet, which was rich in milk. It was particularly encouraging that the weight gains were on the whole better in the second half of the trial than in the first half, because signs of intolerance and ill effects, if there were any, might well be expected to increase with time. The clinical condition of the children steadily improved through the trial, and at the end was quite good; a similar improvement occurred in the children given cow's milk. Recovery from the many attacks of infectious illness was as good in one group as in the other as far as could be judged.

Haemoglobin. Estimations of haemoglobin were made by the Haldane method at the beginning and end of the trial. The results are shown in Table 28. Some of the children, who were adjudged anaemic by the Home doctor, were

TABLE 28

Haemoglobin values for children of from 1 to 2 years old in Trial I in the Augustinusstift

	Mixture A diet				Mixture B diet				Cow's milk diet		
	Haemoglobin percentage				Haemoglobin percentage				Haemoglobin percentage		
Name	at beginning of trial	at end of trial	alteration	Name	at beginning of trial	at end of trial	alteration	Name	at beginning of trial	at end of trial	alteration
Simson	Fe*			Annelie	77	86	+9	Laurenz	62	66	+4
Hans Günther	Fe			Diethard	69	75	+6	Gordona	Fe		
Ingrid	86	76	−10	Detlef	74	79	+5	Margret	88	72	−16
Udo	77	79	+2	Eva	Fe			Hans	Fe		
Wolfgang	79	70	−9	Isette	Fe			Emilie	74	83	+9
Annemarie	90	83	−7	Ruprecht	73	77	+4	Brigitte	Fe		
Heinz	98	93	−5	Gerda	82	85	+3	Horst	82	76	−6
				Liselotte	Fe			Petrus	68	62	−6
				Hans Josef	77	91	+14	Sophie	92	69	−23
				Adelheid	95	85	−10	Günther	66	66	0
				Hans Peter	93	82	−11	Lili	Fe		
				Bernhard	Fe			Roswitha	66	58	−8

* Fe indicates that iron therapy was given during the trial.

given iron therapy, and the results of the estimations done on them have, therefore, been omitted. The children are listed in descending order of weight gain at the end of the trial, as in Table 27.

Two conclusions may be drawn. Poor gains in weight were to some extent associated with a fall in haemoglobin value, and the diet containing Mixture B usually produced a rise in haemoglobin value which was not found in the other feeding groups. The observation is consistent with the results of analysis (Table 15, p. 61), which show that Mixture B contained much more iron than Mixture A.

Trial II

It was felt at the end of Trial I that although the diet containing Mixture B had been satisfactory, there was still room for improvement, and it was expected with some confidence that the addition of small amounts of dried skimmed cow's milk would yield results fully equal to those obtained with the whole milk diet.

Trial II began on April 3, 1948, and lasted 24 weeks until September 24, 1948. There were three feeding groups; one received Mixture B1 containing 87·5 per cent of Mixture B with 12·5 per cent of dried milk, and one Mixture B2 containing 75 per cent of Mixture B with 25 per cent of dried milk. It was realized that the use of these combinations was in one way a retrograde step, because the proportion of the cereal and soya mixture in the diets would be slightly reduced. The third group received cow's milk.

The results are given in Table 29. They show that the children who received Mixture B2 grew exceptionally well, and possibly better than those who received the cow's milk diet. All the children who were fed with Mixture B2 for the whole 24 weeks of the trial, except one who was ill in the last weeks, exceeded the standard weight gain. The gains were remarkably consistent.

There was very little gastro-intestinal upset. One child (Barnabas) reacted to the cereal, soya and milk mixture in a way that had not previously been seen.

TABLE 29

Performance of children of from 1 to 2 years old in the Augustinusstift, expressed as change in percentage of standard body weight and as ratio of actual to standard body weight gain

Trial II

Supplement to diet	Name	Sex	Age at beginning (weeks)	Percentage of standard weight			Ratio of actual to standard weight gain				Remarks
				at beginning	after 24 weeks	alteration	from 1st to 8th weeks	from 9th to 16th weeks	from 17th to 24th weeks	from 1st to 24th weeks	
Mixture B1 Malted barley, wheat, and soya flour; 87·5 parts mixture and 12·5 parts skimmed milk. Steamed.	Horst	M	90	88	98	+10	3·73	1·14	1·65	2·17	Throat infection in 14th week.
	Diethard	M	104	84	88	+4	1·27	1·50	1·52	1·42	Large child, over standard weight.
	Margret	F	100	101	105	+4	1·21	1·44	0·65	1·38	Attacks of diarrhoea in 4th and 9th weeks. Throat infection in 17th week.
	Hans Günther	M	105	77	81	+4	1·31	0·32	2·36	1·30	Always a difficult child.
	Harry	M	77	73	74	+1	1·06	1·10	0·30	0·84	*Grippe* in 10th week. Throat infection in 20th week. Over standard weight.
	Friedel	M	64	101	103	+2	3·42	0·73	negative	0·81	
	Ruprecht	M	97	95	93	−2	1·35	2·25	negative	0·57	*Grippe* in 6th week. Diarrhoea in 18th and 21st weeks.
	Günther	M	86	101	96	−5	1·76	0·65	negative	0·52	Over standard weight. Throat infection in 22nd week caused loss of 1·0 kg.
	Lili	F	73	90	—	—	1·68	1·32	—	—	*Grippe* and diarrhoea in 16th week. Changed to milk diet.

Mixture B2
As above, but with 75 parts mixture and 25 parts skimmed milk.

Name	Sex									Remarks
Liselotte	F	79	96	113	+17	4·30	3·35	2·08	3·15	Throat infection in 12th week.
Hannelore	F	66	98	108	+10	2·50	1·15	2·29	2·04	
Eva	F	83	81	90	+9	2·10	0·93	2·69	1·90	
Sophie	F	92	88	94	+6	1·87	1·08	2·80	1·86	
Adelheid	F	107	107	110	+3	2·23	1·00	1·49	1·51	
Wolfram	M	81	86	96	+10	2·50	1·87	0·59	2·05	*Grippe* in 15th week. Throat infection in 23rd week.
Hans	M	92	103	106	+3	3·06	0·78	0·38	1·39	Diarrhoea in 6th week. Throat infection in 18th week. Subsequently diagnosed as T.B.
Alberich	M	72	80	82	+2	0·78	1·95	0·77	1·10	Difficult and nervous child. Poor feeder throughout.
Johannes	M	66	99	98	−1	0·77	2·60	negative	0·87	*Grippe* in 4th week. Diarrhoea in 20th week. Very near standard weight.
Barnabas	M	57	102	107	+5	1·30	1·06	0·94	—	Vomiting always caused by *Brei* containing more than 50 per cent of cereal and soya mixture. Appetite good throughout.
Udo	M	92	74	78	+4	negative	5·24	0·54	—	Loose stools in 6th week, with loss of 1·30 kg. Changed to cow's milk diet, but weight gains still poor.
Laurenz	M	106	77	—	—	0·01	2·12	—	—	Appetite poor in first weeks. Loose stools in 22nd week. Changed to milk diet.

Cow's milk

Name	Sex									Remarks
Ingrid	F	94	96	108	+12	2·78	3·30	1·58	2·57	
Roswitha	F	90	78	89	+11	2·26	2·28	2·80	2·41	
Brigitte	F	74	95	100	+5	negative	1·36	1·52	1·70	*Grippe* in 7th week.
Klaus	M	68	85	92	+7	1·63	1·11	1·86	1·53	Ear infection and diarrhoea in 15th week.
Franz	M	93	76	81	+5	2·00	0·65	1·27	1·31	
Karl Heinz	M	58	98	103	+5	1·67	1·92	0·89	1·30	Loss of appetite from 18th to 20th weeks.
Heinz	M	81	97	98	+1	1·51	0·61	0·65	0·96	Thrush from 15th to 18th weeks.
Petrus	M	104	79	80	+1	1·41	1·09	negative	0·86	Throat infection and diarrhoea from 22nd to 24th weeks.
Hans Josef	M	94	75	77	+2	negative	1·98	1·11	0·86	Many minor infections. Appetite always variable.

He ate well and with obvious enjoyment, but half an hour after the meal he vomited its undigested remains. He did so repeatedly on numerous occasions and only ceased when 50 per cent of the milk *Brei* was incorporated with 50 per cent of the Mixture B2 *Brei*. Attempts to increase the proportion of the latter always resulted in vomiting and it was clear that the cereal, soya and milk mixture contained some ingredient which the stomach of this one child could not tolerate. One other child (Udo), who began well and after four weeks had gained weight excellently, began in the sixth week to have loose stools, and after many unsuccessful attempts had been made to relieve the condition, had finally to be given the cow's milk diet. Even then he continued to give trouble, and failed to grow well. He was a nervous and difficult child, who could only with some generosity be considered normal. One child (Laurenz) who was notorious for being liable to gastro-intestinal upsets, had a particularly severe attack of uncertain origin in the 22nd week of the trial and had to be given buttermilk and other therapeutic agents.

The weight gains of the children who had Mixture B1 were not quite as good as those of the children who received the cow's milk diet. Four children had attacks of loose stools which may have been signs of intolerance. They were not serious, although they produced temporary setbacks to the weight gain, and only one of the four children (Lili) had to be transferred to the cow's milk group; she grew well in spite of intestinal upsets, but consistently demonstrated her reluctance to take the cereal, soya and milk mixture.

The children were clinically in very good condition, and at the end of the trial no difference between the groups could be detected. At various times during the trial, the Augustinusstift was visited by British doctors with experience of children. They all expressed their surprise at the excellent state of the children, and were unable to decide from appearance whether any given child was receiving the diet with milk or with one of the cereal and soya mixtures.

A factor of some importance, realized for the first time in the course of Trial II, was the difference in the degree of success achieved by the different wards in feeding their children with the cereal and soya mixtures. One ward, in particular, seemed to find much trouble and, since it held many of the children aged between 1 and 2 years old at this time, the results of the trial as a whole were undoubtedly affected. Fortunately, the distribution of the children from this ward through the three feeding groups was fairly even, and the harmful effects on the results for any one group were, therefore, reduced. It was probably no coincidence that the children who occupied the lowest places in the list of weight gains in all three groups were in this one ward.

Trial III

In Trial III the cereal and soya Mixtures C and C2, originally intended for the children, were altered after eight weeks to Mixture D1, for the same reasons, and in the same way, as for the children under 1 year (p. 79). The whole trial lasted sixteen weeks, from September 25, 1948, to January 15, 1949. The changes in diet were made on November 26. They consisted of the substitution of the cereal, soya and milk Mixture D1 (a maize, malted barley, soya and 10 per cent skimmed milk mixture) for the Mixtures C and C2, which contained wheat not maize flour. Mixture C2 contained 10 per cent of skimmed milk. In all three mixtures the trypsin inhibitor had been destroyed. The diet of the children receiving cow's milk remained unchanged.

First eight weeks. The results are given in Table 30.

The weight gains of those having Mixture C2 were perhaps slightly more consistent than of those having Mixture C, and were approximately the same as of those having cow's milk. The results were not altogether satisfactory, because of the occurrence of loose stools. Seven of the fourteen children having Mixture C, eight of the twelve having Mixture C2, and four of the twelve having cow's milk, were affected; much of the trouble was undoubtedly of infective origin, but the mixtures were held to be partly responsible. Even when the children in the Mixture C and C2 groups were quite well, they had a slightly higher average number of stools each day than the children in the cow's milk group, and they seemed to be more sensitive to the infection. There was no

TABLE 30

Performance of children of from 1 to 2 years old in the Augustinusstift, expressed as change in percentage of standard body weight and as ratio of actual to standard body weight gain
Trial III: first 8 weeks

Supplement to diet	Name	Sex	Age at beginning (weeks)	Percentage of standard weight			Ratio of actual to standard weight gain	Remarks
				at beginning	after 8 weeks	alteration		
Mixture C	Bianca ..	F	98	105	113	+8	4·60	
Malted barley, wheat	Florenz ..	F	68	90	98	+8	3·10	
and soya flour.	Cosima ..	F	83	90	96	+6	2·97	Diarrhoea in 5th week.
Trypsin inhibitor	Mathilde ..	F	75	86	92	+6	2·80	Diarrhoea in 5th week.
removed by pro-	Alfred ..	M	106	81	85	+4	2·16	Chronic sepsis of fingers.
longed steaming.	Günther ..	M	111	100	102	+2	1·50	
	Laurenz ..	M	132	79	80	+1	1·42	Chronic loose stools. Did not gain after 4th week.
	Liselotte ..	F	103	114	115	+1	1·27	
	Diethard ..	M	130	87	88	+1	1·13	
	Horst ..	M	115	98	95	−3	negative	Diarrhoea in 5th week.
	Roswitha ..	F	115	87	84	−3	negative	Diarrhoea in 5th week.
	Erika ..	F	75	98	95	−3	negative	Diarrhoea in 5th week.
	Alberich ..	M	97	84	82	−2	negative	Diarrhoea in 5th week.
	Johannes ..	M	91	99	92	−7	negative	Throat infection in 6th week.
Mixture C2	Hannelore ..	F	91	106	113	+7	3·25	
Same as above but	Margret ..	F	126	103	106	+3	2·24	
with 10 per cent	Norbert ..	M	80	96	100	+4	2·14	Diarrhoea in 3rd week.
dried skimmed milk.	Stephan ..	M	94	83	87	+4	2·10	
	Klaus ..	M	93	90	93	+3	1·98	
	Barbara ..	F	82	88	91	+3	1·74	Diarrhoea in 3rd week.
	Hans Josef ..	M	120	77	79	+2	1·58	Diarrhoea in 3rd week.
	Sara ..	F	64	112	112	0	1·50	Diarrhoea in 5th week.
	Ingrid ..	F	117	108	107	−1	0·50	Diarrhoea in 5th week.
	Eva ..	F	109	85	85	0	0·40	Began trial in middle of attack of diarrhoea and never really recovered.
	Hedwig ..	F	68	101	98	−3	0·39	Many attacks of diarrhoea.
	Hans Günther	M	129	79	78	−1	0·13	Diarrhoea in 5th week.
Cow's milk	Udo ..	M	117	77	82	+5	2·70	
	Kunigunde ..	F	117	96	101	+5	2·50	
	Franz ..	M	118	81	84	+3	2·50	
	Harry ..	M	102	73	76	+3	1·81	Diarrhoea in 5th week.
	Michael ..	M	64	91	95	+4	1·81	Diarrhoea in 6th week.
	Heinz ..	M	107	98	99	+1	1·52	Diarrhoea in 5th week.
	Ruprecht ..	M	123	96	98	+2	1·45	
	Hubert ..	M	66	92	92	0	0·92	Throat infection in 5th week.
	Therese ..	F	94	92	92	0	0·74	Diarrhoea in 5th week.
	Barnabas ..	M	82	106	106	0	0·65	Child over standard weight.
	Petrus ..	M	130	80	77	−3	negative	Ear infection in 6th week.
	Friedel ..	M	90	113	109	−4	negative	Ear infection in 4th week.

adverse effect unless the number of stools was excessive, but a change of diet was deemed advisable. Various therapeutic measures were tried, but the only one found really effective was the addition to the Mixture C and C2 diets of considerable amounts, about 25 per cent, of cow's milk *Brei*. Glucose, even in amounts great enough to bring the ratio of maltose to glucose near to unity, dried buttermilk, and kaolin did not have the same good effect.

Second eight weeks. In the second part of the trial there were only two feeding groups, of which one received the cereal, soya and milk Mixture D1 and the other cow's milk. The change from Mixtures C and C2 was made between one meal and another, and almost at once there was a reduction in the number of complaints of loose stools. The mixture always seemed to produce softer stools than the milk, but the number of stools was not unduly large. The weight gains (Table 31) were on the whole better in those having Mixture D1

TABLE 31

Performance of children of from 1 to 2 years old in the Augustinusstift, expressed as change in percentage of standard body weight and as ratio of actual to standard body weight gain

Trial III: second 8 weeks

Supplement to diet	Name	Sex	Age at beginning (weeks)	Percentage of standard weight			Ratio of actual to standard weight gain	Remarks
				at beginning	after 8 weeks	alteration		
Mixture D1	Liselotte	F	111	115	119	+4	3·23	
Malted barley, maize	Diethard	M	138	88	93	+5	3·20	
and soya flour; 10	Günther	M	119	102	105	+3	2·53	
per cent dried skim-	Margret	F	134	106	109	+3	2·11	
med milk. Trypsin	Horst	M	123	95	98	+3	2·06	Diarrhoea in 7th week.
inhibitor removed	Hans Günther	M	137	78	81	+3	1·97	Thrush in 7th week.
by prolonged heat-	Alberich	M	105	82	85	+3	1·89	Diarrhoea in 2nd week.
ing.	Norbert	M	88	100	102	+2	1·41	
	Florenz	F	76	98	98	0	0·91	Throat infection in 1st week
	Bianca	F	106	113	112	−1	0·80	Throat infection in 4th we
	Roswitha	F	123	84	84	0	0·78	*Grippe* in 8th week.
	Ingrid	F	125	107	105	−2	0·25	
	Barbara	F	90	91	86	−5	negative	Diarrhoea in 8th week.
	Cosima	F	91	96	91	−5	negative	Diarrhoea in 8th week.
	Alfred	M	114	85	81	−4	negative	Chronic sepsis of fingers.
Cow's milk	Barnabas	M	90	106	112	+6	3·27	
	Petrus	M	138	77	82	+5	3·24	
	Ruprecht	M	131	98	102	+4	3·03	
	Hubert	M	74	92	100	+8	3·00	
	Friedel	M	98	109	112	+3	2·02	
	Therese	F	102	92	93	+1	1·57	
	Kunigunde	F	125	101	101	0	1·02	
	Michael	M	72	95	94	−1	0·70	Frequent attacks of diarrh
	Heinz	M	115	99	94	−5	negative	Diarrhoea in 5th week from time to time afterwa
	Udo	M	125	82	77	−5	negative	Appetite capricious. Freq attacks of diarrhoea.
	Franz	M	126	84	80	−4	negative	
	Harry	M	110	76	73	−3	negative	

than in those having cow's milk, but they are difficult to assess because there was again an outbreak of infective diarrhoea.

In spite of the complications probably introduced by faults in the manufacture of the mixtures, it was felt that the removal of the trypsin inhibitor from the soya flour had proved valuable. It was obvious, however, that the

factors responsible for variations in the character of the mixtures had not been fully controlled.

Near the end of the trial there was an epidemic of thrush, but it was remarkable that there was not usually any accompanying loss of appetite or weight. *Brei* was substituted for most of the bread in the diets because it had less abrasive action on the sore gums and buccal mucous membrane.

Summary of Trials I, II and III with Children of from 1 to 2 Years in the Augustinusstift

The series of trials with children of from 1 to 2 years produced results which were in some ways more definite than those obtained with the younger children.

The composition of the diets used in the trials is summarized in Table 32.

TABLE 32

Children of from 1 to 2 years old in the Augustinusstift: average values for the diets eaten in Trials I, II and III and the distribution of calories among the various items of the diet

Sources of calories	Trial I		Trial II		Trial III			Trials I, II, III
	Mixture A diet	Mixture B diet	Mixture B1 diet	Mixture B2 diet	Mixture C diet	Mixture C2 diet	Mixture D1 diet	Cow's milk diet
Cal. per kg. body weight from:								
Protein	11	15	15	17	14	15	18	11
Fat	14	18	16	12	17	19	18	23
Carbohydrate	99	80	74	74	72	69	72	67
Total	124	113	105	103	103	103	108	101*
Percentage of total cal. from:								
Protein	9	13	14	16	13	15	14	11
Fat	11	16	15	12	18	18	17	24
Carbohydrate	80	71	71	72	69	67	69	65
Percentage of total cal. from:								
Cow's milk	0	0	5	9	0	4	4	33
Cereal and soya mixture	47	48	41	39	54	51	42	0
Semolina	26	27	29	30	14	15	24	45
Vegetables	10	10	11	10	9	8	8	11
Bread	11	9	8	8	15	14	14	6
Butter	6	6	6	4	8	8	8	5
Percentage of total-protein cal. from:								
Cow's milk	0	0	14	28	0	12	9	59
Cereal and soya mixture	52	67	54	48	73	64	58	0
Semolina and bread	48	33	32	24	27	24	33	41
Percentage of total cal. from:								
Cow's milk protein	0	0	2·6	4·6	0	1·7	1·5	6·6
Cereal and soya mixture protein	4·9	9·0	7·5	7·8	9·7	9·3	9·8	0
Number of diets averaged	8	14	8	9	9	13	11	

* 114 in Trial I.

Except in the diet with Mixture A the percentage of total calories from protein was always higher in the cereal and soya mixture diets than in the milk diet.

Diets not containing Milk

There was no doubt at all that under the conditions in which it was used, so that it provided nearly 50 per cent of the total calories in a diet containing no milk, Mixture A was unsatisfactory, chiefly because it caused gastro-intestinal upsets. When used in exactly the same way, Mixture B was, on the

contrary, very satisfactory. The two mixtures differed not merely in the proportions of their ingredients, but also in their methods of manufacture. It was almost certain that a fault in manufacture was partly responsible for the failure of Mixture A. The fault may have been in the drying, because in Trial III material which had been overheated was found to be noxious in much the same way. The third of the diets which contained no milk, that made up with Mixture C, was probably reduced in value by the overheating of the mixture, but nevertheless was effective. The results of using the three diets are shown graphically side by side in Fig. 3(a). Compared in this way, the results show a slight advantage in favour of Mixture C over Mixture B, and, since the chief difference lay in the removal of the trypsin inhibitor from the soya used for Mixture C, it appears that the removal was beneficial.
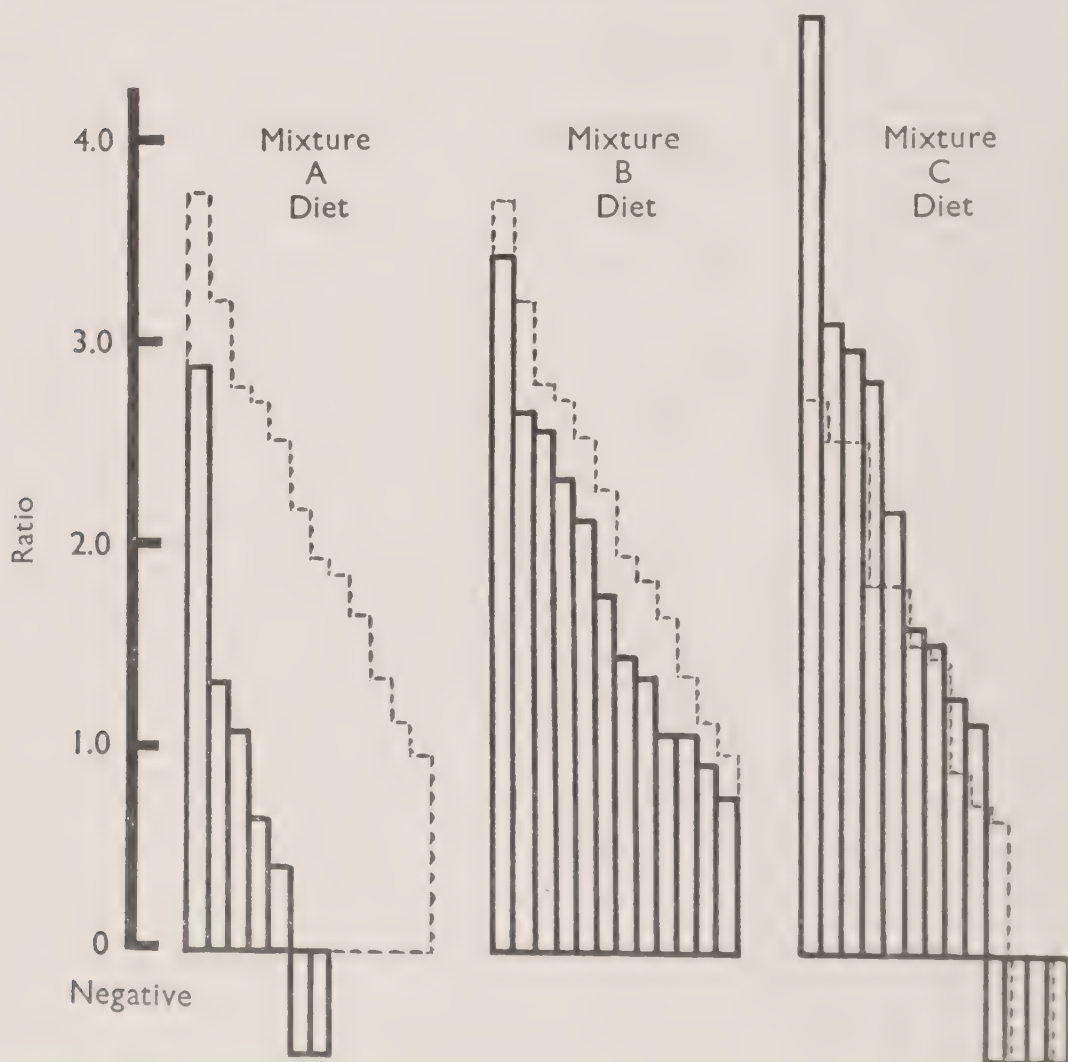
FIG. 3(a).

Ratios of actual to standard weight gains of children of from 1 to 2 years old given the cereal and soya mixture diets which did not contain any milk. The dotted lines indicate the ratios of the children given the cow's milk diet.

MIXTURE A.   Malted barley, wheat and soya flours. No dried milk. Short steaming.
MIXTURE B.   Same as Mixture A. Longer steaming.
MIXTURE C.   Same as Mixture B but steamed long enough to remove the trypsin inhibitor.

Diets containing Milk

In the diets supplemented with Mixtures B1, B2 and D1, the cereal and soya part of the mixtures supplied about 40 per cent of the total calories, and with Mixture C2 about 50 per cent; the amounts of milk in the four diets supplied 5, 9, 4 and 4 per cent of the total calories. The results obtained with Mixture B1 when seen beside the others (Fig. 3(*b*)), seem to be a little inferior; those with Mixture B2 are perhaps the best of all, but those with Mixtures C2 and D1 are almost equally good. The Mixture C2 and D1 diets contained much less milk than the Mixture B2 diet, and it seems justifiable to conclude that the
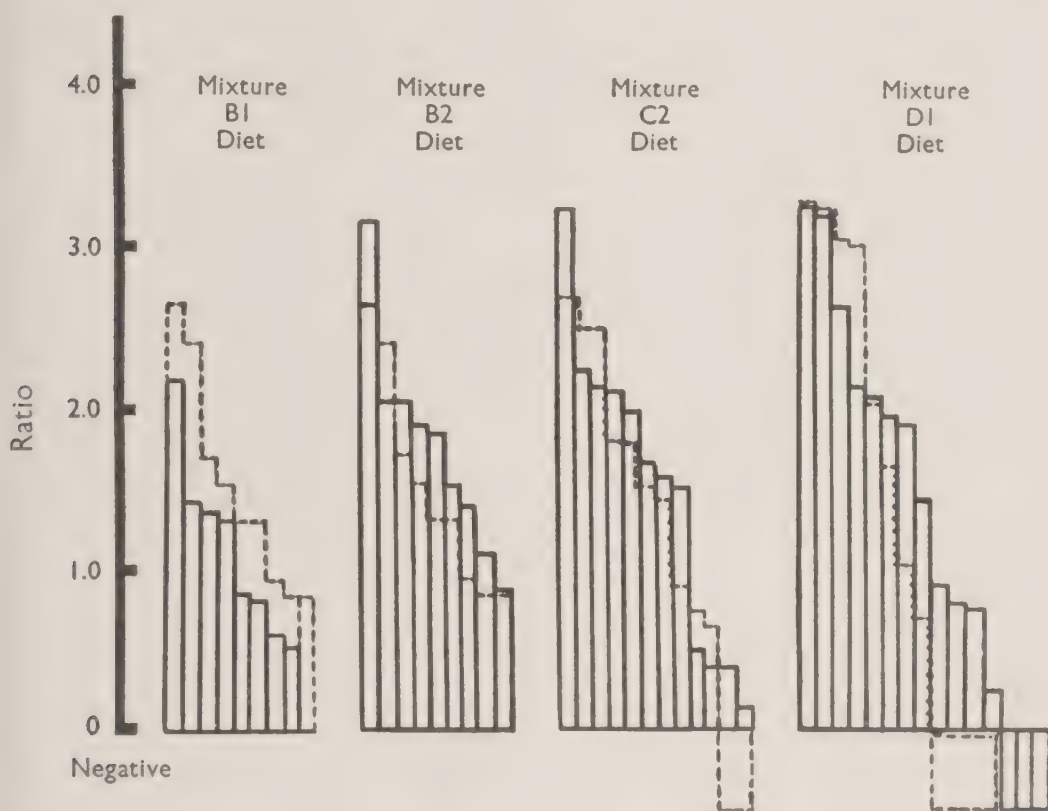
Fig. 3(*b*).

Ratios of actual to standard weight gains of children of from 1 to 2 years old given the cereal and soya mixture diets which contained some milk. The dotted lines indicate the ratios of the children given the cow's milk diet.

MIXTURE B1.   Malted barley, wheat and soya flour; skimmed milk powder 12½ per cent.   Moderate heating.
MIXTURE B2.   As Mixture B1 but with 25 per cent skimmed milk powder.
MIXTURE C2.   Malted barley, wheat and soya flour with 10 per cent skimmed milk solids.   Heated to remove trypsin inhibitor.
MIXTURE D.   As Mixture C2 but maize instead of wheat flour.

removal of the inhibitor was as advantageous as adding a considerable amount of milk, possibly more than half of the 25 per cent which was included in Mixture B2. One discrepancy needs special comment. When in Trial II Mixture B was fortified with 12½ per cent milk, it did not give results which were obviously superior to those obtained in Trial I with Mixture B, unfortified. The only explanations that can be offered are that 12½ per cent of dried milk was not a sufficiently large amount to make any obvious improvement, or that

the mixture as supplied for the two trials differed in some unknown way, that used in Trial II being of slightly lower quality.

GENERAL SUMMARY OF TRIALS WITH CHILDREN OF FROM 6 MONTHS TO 2 YEARS OLD

The provision of an adequate transitional diet to bridge the gap between breast milk and the adult diet presents great difficulty if no milk at all is available. The results obtained with children up to 2 years old have, therefore, considerable importance. Of all the cereal and soya mixtures used, only Mixture A gave results which were really poor; even Mixture C2, which like Mixture A was discarded, was successful in that it produced growth exceeding the standard in the majority of children. All the other five diets, used for short periods or long, and irrespective of whether they included cow's milk or not, usually gave excellent growth.

SOME SELECTED EXAMPLES OF THE PROLONGED USE OF THE CEREAL AND SOYA MIXTURES IN THE DIETS OF CHILDREN OF FROM 6 MONTHS TO 2 YEARS OLD

It seemed worth while to set out in full some specimen records of children in the Augustinusstift having the cereal and soya mixtures for a prolonged period. The selected records are given graphically in the form of weight charts which show the actual weight in relation to the standard weight and calorie intake, and the coincidence of certain events with alterations in the weight curves. Most of the diagrams (Fig. 4(a) to (f)) relate to children who in Trial I were given Mixture B and who took part at least in Trials I and II and some of them also in Trial III.
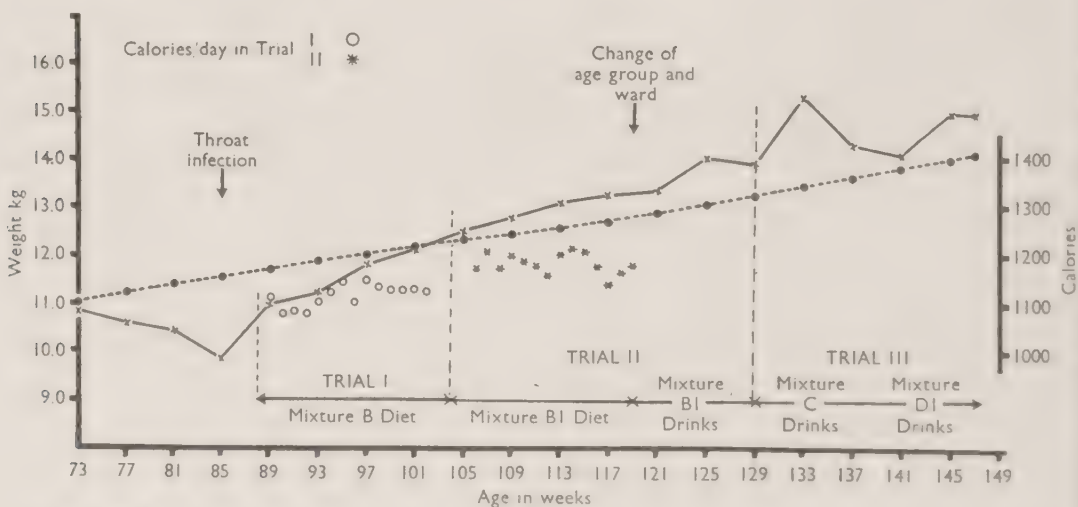
FIG. 4(a).

ANNELIE.

···●···●···, standard weight

—×—×—, actual weight

In the weeks before Trial I the child lost weight during a prolonged gastro-intestinal upset and the starting weight was therefore low. She throve on the Mixture B diet and by the end of the trial was over the standard weight.
She received cereal and soya mixtures in the subsequent trials and the weight gains were good.
The calorie intakes showed the usual rather low values characteristic of the child whose weight is near the standard weight.
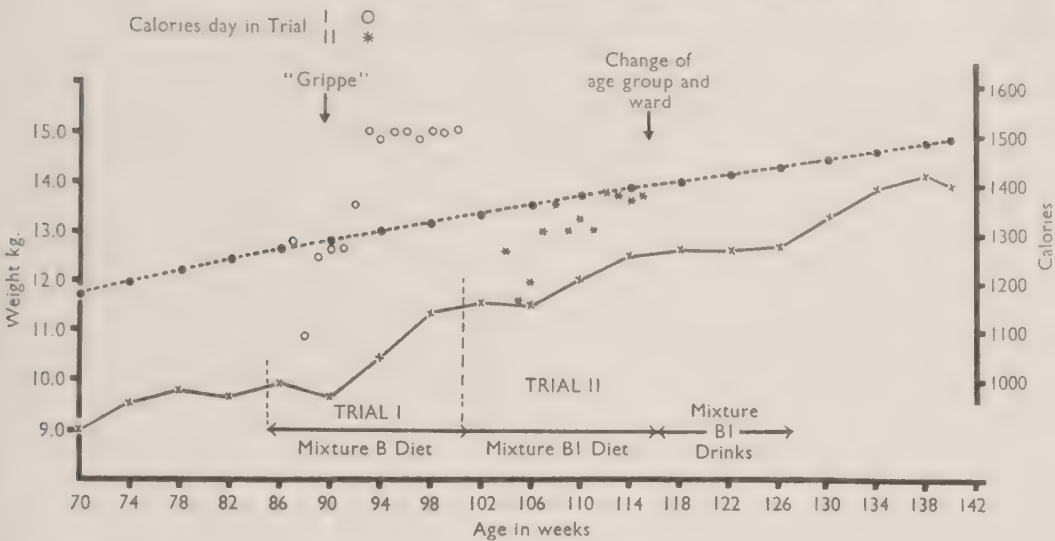
FIG. 4(b).

DETLEF.

Shortly after the start of Trial I the child had an attack of *Grippe* accompanied by diarrhoea and vomiting. He recovered well and gained weight satisfactorily until the end of the trial. His calorie intake was high, about 125 per kg. body weight.

In Trial II he was given Mixture B1 until he joined the group of children of from 2 to 5 years old. He was then 91 per cent of the standard weight and had gained 13 per cent since the beginning of Trial I. His calorie intake per kg. was much lower than it had been in Trial I. His record in Trial II is not included in Table 29 because of the change of age group.
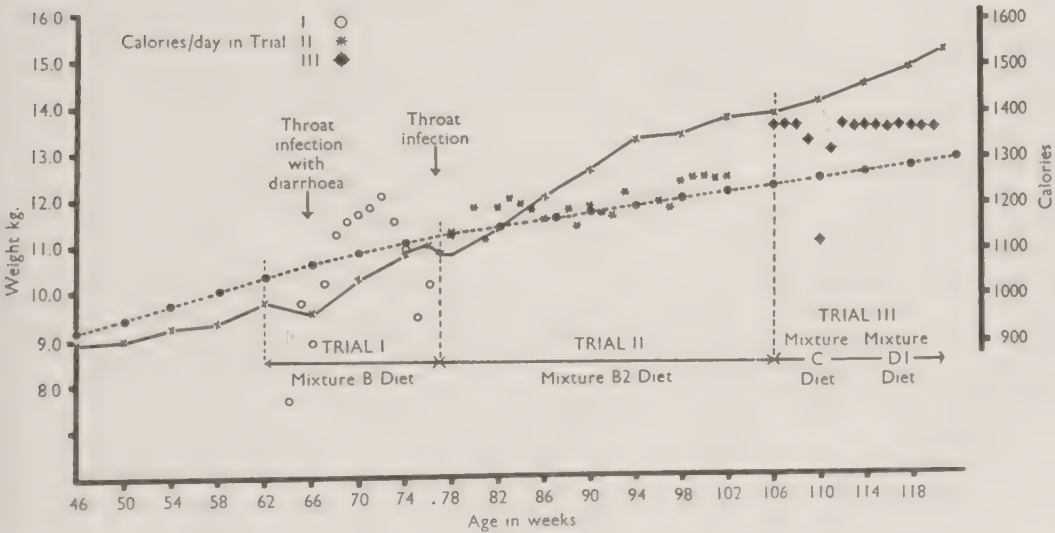
FIG. 4(c).

LISELOTTE.

Sixteen weeks before Trial I began the child's weight was 98 per cent of the standard. In the first few weeks there was an attack of tonsillitis accompanied by diarrhoea. Subsequent weight gains were good until the last few weeks of the trial when another attack of tonsillitis occurred. The weight loss was small, but the reduction in calorie intake was great.

In Trial II progress was excellent on Mixture B2 and the standard weight was far exceeded. There were occasional slight illnesses in Trial III but progress continued to be satisfactory.

······●···●····, standard weight
——x——x——, actual weight

The charts include a period of about fourteen weeks before the beginning of Trial I and show the poor weight gains which were common in the Home at that time when the diet was undoubtedly inadequate (see p. 66). Throughout the whole period of observation they show the extreme sensitivity of the weight to illness, and to change from one ward to another. The calorie intakes usually reflected the variations in weight. When the children were in good health, their calorie intakes bore an interesting relation to the degree of deviation from the standard weight. The overweight children usually ate less food, in proportion to their weight, than the underweight children. The point is discussed later (p. 103).

It is interesting to compare the progress through the trials of the boys Diethard (Fig. 4(e)) and Petrus (Fig. 4(f)) because they were identical twins. Diethard always had a cereal and soya diet and Petrus always had a milk diet. Diethard certainly made the better progress.
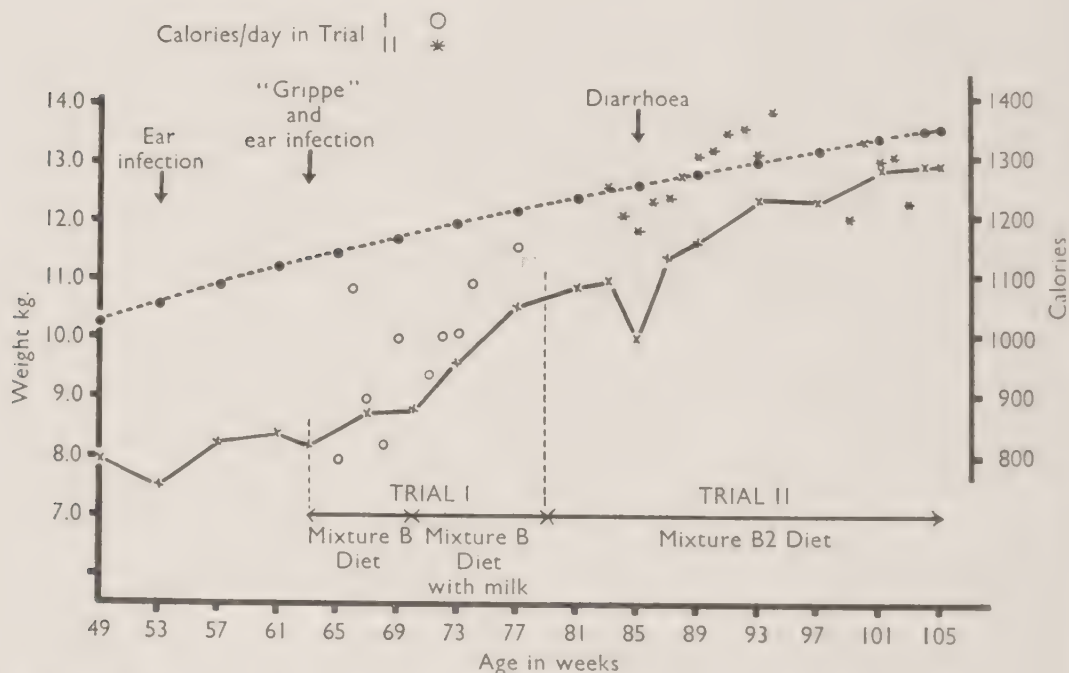
FIG. 4(d).

WOLFRAM.

···●···●···, standard weight

—×—×—, actual weight

The weight gains of the child before Trial I began were not satisfactory owing to a recurrent ear infection, and in the first weeks of the trial they continued to be poor. Mixture B tended to produce rather loose stools and eventually it was decided to change the diet by incorporating 25 per cent cow's milk *Brei* with 75 per cent of Mixture B *Brei*. Immediate improvement followed. The percentage of the standard weight was only 74 when the diet was changed but was 90 at the end of the trial.

In Trial II Mixture B2 was given. Shortly after the start there was an attack of diarrhoea in which 1·0 kg. was lost. Subsequent progress was good although the child was always liable to have loose stools.

The calorie intake per kg. body weight was rather high, about 112.

At the beginning of Trial I the weight was 72 per cent of the standard; at the end of Trial II it was 96 per cent.

Calories/day in Trial I   ○
                       II   *
                       III ◆

"Grippe"

Weight kg

Calories

TRIAL I
Mixture B Diet

TRIAL II
Mixture B1 Diet

TRIAL III
Mixture   Mixture
C   D1
Diet   Diet

Age in weeks
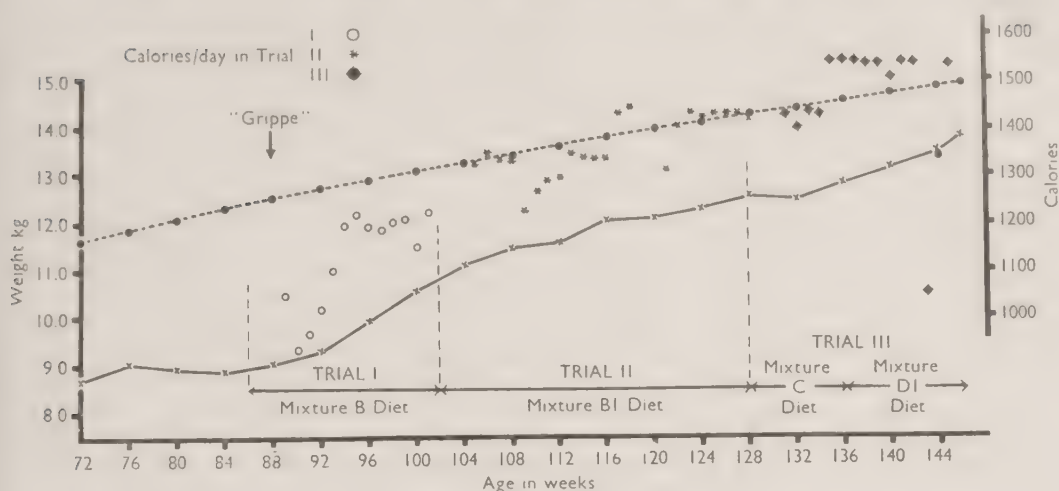
FIG. 4(*e*).

DIETHARD.

In the 14 weeks before Trial I the child gained in weight only one fourth of the standard amount.   The start of the Trial was poor owing to an attack of *Grippe* but afterwards weight was gained rapidly.

In Trial II Mixture B1 was given and the weight gains continued to be good, although not quite as rapid as before.   The child gained weight steadily in Trial III also, when he had Mixture C and Mixture D1.

From the beginning of Trial I to the end of Trial III the percentage of standard weight changed from 72 to 93; the gain in the period was nearly twice the standard gain.

The child was the identical twin brother to Petrus (*Fig.* 4 (*f*)), who had the milk diet throughout the trials.   Both children took from 120 to 130 Calories per kg. body weight.

Calories/day in Trial I   ○
                       II   *
                       III ◆

"Grippe"

Weight kg.

Calories

TRIAL I
Milk Diet

TRIAL II
Milk Diet

TRIAL III
Milk Diet

Age in weeks
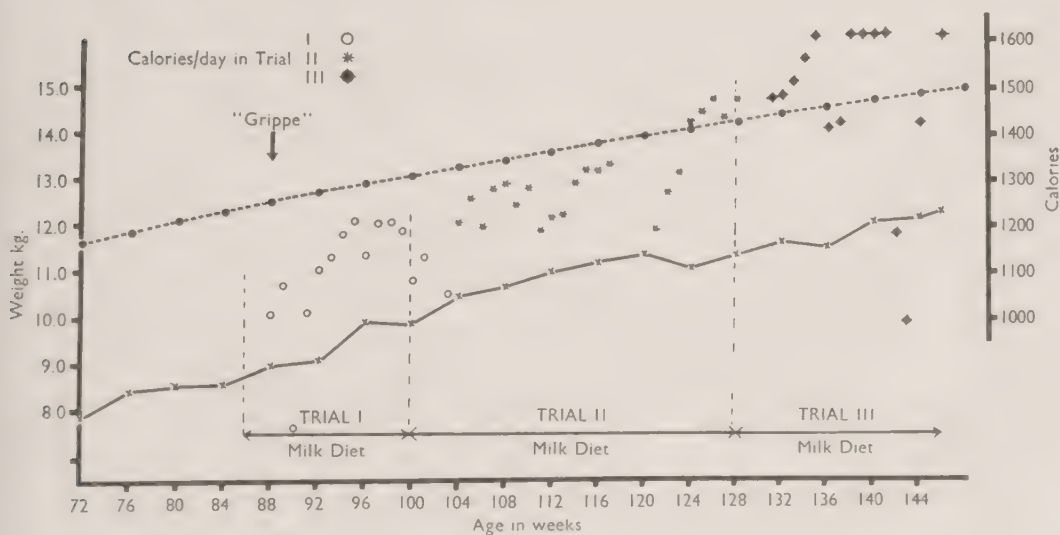
FIG. 4(*f*).

PETRUS.

In the 14 weeks before Trial I the child, unlike his identical twin brother, Diethard, improved his weight to 72 per cent of the standard from 67 per cent.   Like his brother, he made a poor start because of an attack of *Grippe*, but his progress was not as good as his brother's although he was given the milk diet.

In spite of being free from any serious illness, and always having the milk diet, the child never greatly improved.   At the end of Trial III his weight was 82 per cent of the standard.   He had, therefore, made up 10 per cent since the beginning of Trial I, but in the same period his brother had made up 21 per cent.

····●····●····, standard weight
——×——×——, actual weight

CALORIE INTAKES OF THE CHILDREN OF FROM 6 MONTHS TO 2 YEARS
OLD, WHEN FED TO APPETITE, AT FIRST WHEN STILL
UNDERNOURISHED, AND SUBSEQUENTLY WHEN FULLY NOURISHED

It has usually been found that children given milk substitutes made from soya or other plant materials need more calories than children given milk. Contrary to expectation, it was found in the present series of trials that although the calories taken per kg. body weight daily were always lowest in the groups having full-cream milk, the figures for those having the cereal and soya mixtures were not greatly different. For the children of from 6 to 12 months old, the average figure was about 102 for the group having full-cream milk or Mixture B which contained no skimmed milk; for the other groups having Mixtures A, B2, C2 or D1, all of which, except Mixture A, contained skimmed milk, it was about 108.

The children of from 1 to 2 years old in Trial I had high intakes; the group having full-cream milk or Mixture B took about 114 Calories per kg. body weight. Presumably the figures were so high because it was the first trial and the children were at their hungriest. In Trials II and III, the group having full-cream milk took 101 Calories per kg. body weight, and the other groups from 103 to 105, whether the cereal and soya mixture contained skimmed milk or not. The data were obtained from the records of three consecutive weeks in the middle of the trials, when the children were well accustomed to the diets. The values for the calorie intakes were compared with the weights in the second of the three weeks. The method of taking an average was adopted to reduce the effect of the fluctuations in intake which inevitably occur when children are fed to appetite. Children who were ill in the chosen weeks were omitted.

Some further examination of the data has been made, but it has been confined to the groups of children of from 6 to 12 months old having full-cream milk or Mixtures A, B or B2, and to the groups of children of from 1 to 2 years old having Mixtures B, B1 or B2. Data obtained with the other supplements were excluded because the mixtures were unsatisfactory, or were given only for short periods.
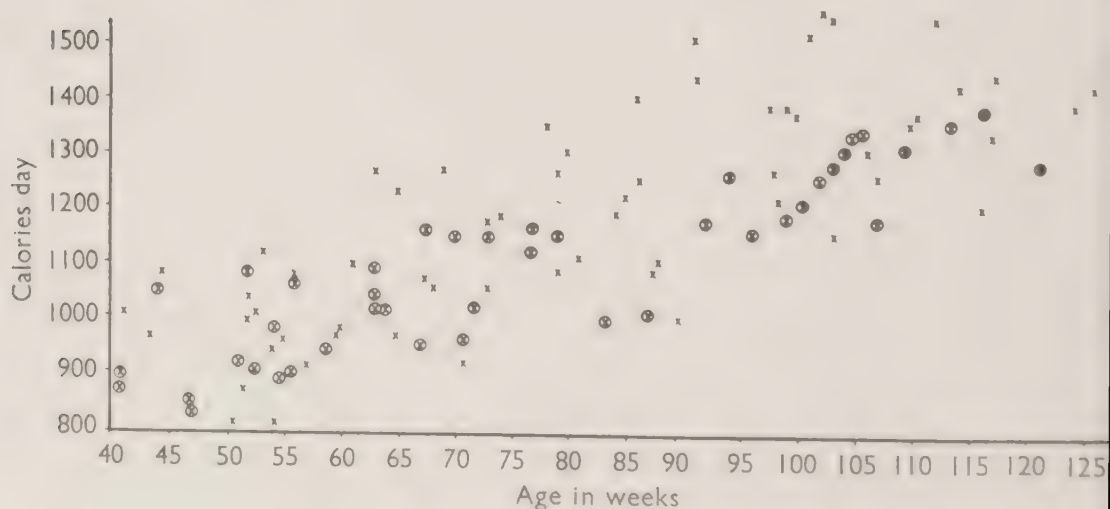
FIG. 5(a).

Number of calories taken daily by children of from 40 to 125 weeks old: boys, crosses; girls, crosses in circles. The intakes increased with age although the intakes per kg. did not (see Fig. 5(c)).

For children aged from 40 to 125 weeks, the total calories taken daily are set out in Figs. 5(a) and (b) in relation to age and to percentage of standard weight; in Fig. 5(c) the calories taken daily per kg. body weight are shown in relation to age and to percentage of standard weight.
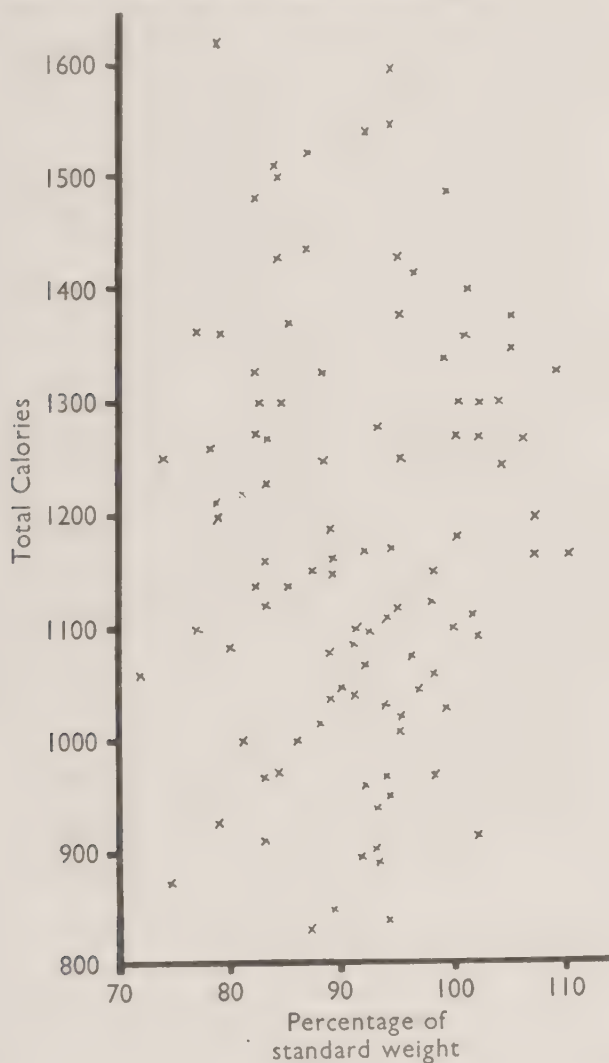
FIG. 5(b).
  Number of calories taken daily by children of both sexes of from 40 to 125 weeks old related to percentage of standard weight.   There was no correlation.

Fig. 5(a) shows that the total calories taken daily, even within such narrow age limits, tended to rise with age. In Trial I the average for children of from 35 to 75 weeks old was 1,000 Calories a day, and for children of from 76 to 125 weeks old it was 1,300 Calories a day; in Trial II the corresponding figures for the two age groups were 1,020 and 1,220 Calories a day. In Widdowson's (1947) studies of individual children's diets, the figures which are most apt for comparison are those for children of from 1 to 2 years old and of from 2 to 3 years old; they are 1,153 and 1,418. Widdowson found no difference in the calorie intake of boys and girls at these ages, and none was found in the present series.

The children differed greatly in the degree to which their weight approached the standard used for comparison; particularly in the first trial, many were

underweight, although even then a few were considerably overweight. It is not surprising, therefore, that there was no correlation between the weight of the child, as a percentage of the standard weight, and the total calories taken (Fig. 5(b)). There was none also between the age of the children and the calories taken per kg. body weight (Fig. 5(c)).
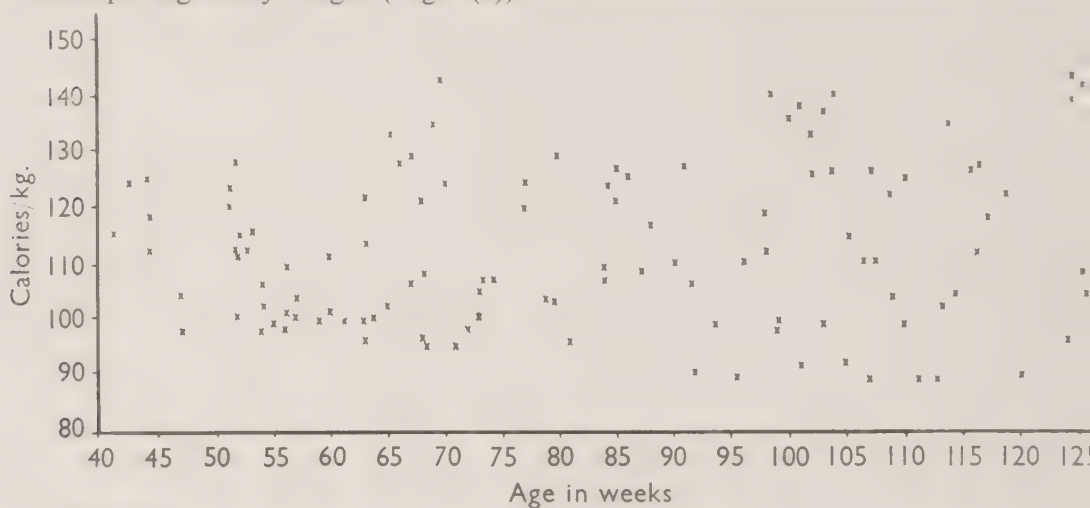
FIG. 5(c).
Number of calories taken daily per kg. body weight by children of both sexes, of from 40 to 125 weeks old. The intakes per kg. body weight did not increase with age.
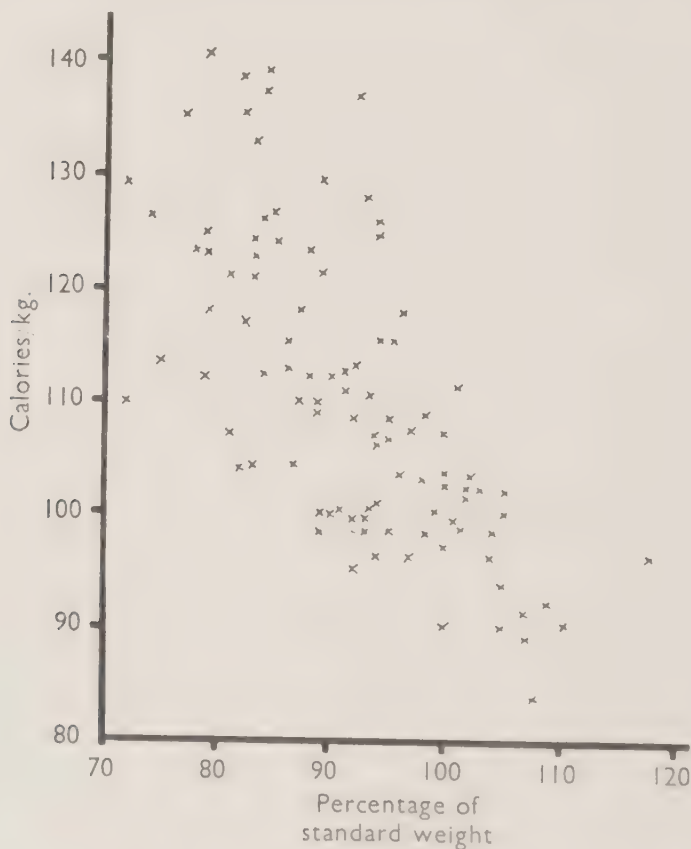
FIG. 5(d).
Number of calories taken daily per kg. body weight by children of both sexes, of from 40 to 125 weeks old, related to percentage of standard weight. The intakes fell as the percentage of standard weight increased.

In contrast with this lack of correlation, there was a close relationship between the number of calories per kg. body weight and the degree of deviation from the standard weight (Fig. 5(d)). In all the trials the children who were most underweight took the greatest number of calories per kg. body weight, and the overweight children the smallest. Fig. 5(d) offers, therefore, a measure of the number of calories which should be supplied in the refeeding of under-nourished children; for children 30 per cent below the standard weight about 130 Calories per kg. are needed, and 10 Calories less for every rise of 10 per cent in the relation to the standard weight. It is recognized in paediatric practice that high calorie diets should be prescribed for children who are underweight (Young, Bishop, Hickman and Williams, 1949), but it is perhaps of value to have the present set of quantitative data from a fairly large number of children, especially as their food intake was unrestricted. It would have been of great interest to give diets containing more protein from milk or some other animal source to see if the calorie intakes would then be further reduced.

Although the children who were the most underweight took the greatest number of calories per unit of weight, they did not increase in weight better than the other children, as can be seen from the results of each trial which are tabulated in descending order of weight gain. The children who occupied the upper places in the lists were not those whose weights were originally furthest below the standard.

RESULTS OBTAINED WITH CHILDREN OF FROM 2 TO 5 YEARS OLD
IN THE AUGUSTINUSSTIFT AND IN THE WAISENHAUS AT DUISBURG

Trial I

There were three groups in Trial I. One received 500 g. daily of fresh whole cow's milk which provided 330 Calories, and the others amounts of the cereal and soya Mixtures A and B of equal calorie value. Mixtures A and B contained malted barley and wheat and soya flours with no skimmed milk powder. Both were heated, but not strongly enough to destroy the trypsin inhibitor. The trial lasted 24 weeks from October 29, 1947, until April 11, 1948.

The children who received Mixture B put on weight rather better than those who received Mixture A, but neither group did quite as well as the group that had fresh cow's milk (Table 33). The Augustinusstift children, particularly those who had the mixtures, grew better than the Duisburg children.

The children at the Augustinusstift were reluctant to drink Mixture A and needed constant persuasion, but Mixture B was well liked, probably because it was not so sweet and had a less malty taste. At the Duisburg Home, where the children seldom seemed reluctant to take food of any kind, there was no such difficulty. At neither Home were there any gastro-intestinal disturbances for which the cereal and soya mixtures might have been responsible, although the stools of the children who had the mixtures were slightly more frequent than those of the children who had cow's milk. There was little illness although the trial ran through the winter, and epidemics such as are common in ordinary schoolchildren did not occur. It was noticeable that minor illnesses, possibly because so little attention was paid to them, seemed to occur less often at the Duisburg Home than at the Augustinusstift.

Haemoglobin. The results of haemoglobin estimations made on the Augustinusstift children are shown in Table 34. The results and conclusions were similar to those for the children aged from 1 to 2 years (p. 86).

TABLE 33

Performance of children of from 2 to 5 years old in the Augustinusstift and in the Waisenhaus at Duisburg, expressed as change in percentage of standard body weight and as ratio of actual to standard body weight gain

Trial I

Supplementary drink	Augustin-usstift (A) or Duisburg (D)	Name	Sex	Age at beginning (months)	Percentage of standard weight			Ratio of actual to standard weight gain
					at begin-ning	after 24 weeks	altera-tion	
Mixture A	A	Edeltraud ..	F	24	93	99	+6	2·17
Malted barley, wheat	A	Theodor ..	M	29	82	88	+6	1·90
and soya flour; no	A	Ute ..	F	34	91	95	+4	1·60
skimmed milk. Short	A	Klaus Peter ..	M	25	99	101	+2	1·40
heating.	A	Franz Josef ..	M	24	91	94	+3	1·33
	A	Augustine ..	F	32	99	100	+1	1·03
	D	Ursule B.	F	39	98	99	+1	1·00
	D	Renate K. ..	F	47	90	90	0	1·00
	D	Peter Z.	M	40	81	81	0	0·93
	A	Gertrud	F	21	115	115	0	0·92
	A	Hans Joachim ..	M	23	87	87	0	0·85
	D	Gisela S. ..	F	26	71	70	−1	0·67
	D	Karl B.	M	36	103	101	−2	0·50
	D	Manfred K. ..	M	47	93	83	−10	negative
	D	Monike G. ..	F	48	76	73	−3	negative
Mixture B	A	Walther	M	39	95	103	+8	2·80
Malted barley, wheat	A	Richard	M	53	88	95	+7	2·37
and soya flour; no	A	Rose	F	35	109	115	+6	2·05
skimmed milk.	A	Elfrida	F	27	97	102	+5	1·69
Longer heating.	A	Rolf	M	27	92	95	+3	1·28
	D	Karl G.	M	25	98	100	+2	1·16
	A	Rudolf	M	21	97	97	0	1·05
	D	Adelheid S. ..	F	43	82	82	0	0·99
	A	Margot	F	23	85	85	0	0·86
	D	Johannes N. ..	M	41	93	93	0	0·80
	A	Volker	M	25	80	80	0	0·79
	D	Wilfrid N. ..	M	41	87	86	−1	0·75
	D	Hugo V.	M	51	92	91	−1	0·66
	D	Elke G.	M	30	88	82	−6	0·01
Cow's milk	D	Inge G.	F	46	112	123	+11	3·60
	A	Martin	M	31	84	93	+9	2·51
	A	Hans Werner ..	M	28	95	103	+8	2·44
	D	Günther M. ..	M	43	101	107	+6	2·26
	A	Dagmar	F	24	82	91	+9	2·23
	A	Wilfrid	M	24	92	100	+8	2·00
	A	Reinhard ..	M	25	92	99	+7	2·00
	A	Hermann ..	M	18	90	98	+8	1·75
	D	Lothar L. ..	M	40	86	89	+3	1·60
	D	Ulrika G. ..	F	37	97	100	+3	1·57
	A	Rudi	M	25	83	86	+3	1·32
	A	Karin	F	28	98	100	+2	1·32
	D	Peter H.	M	38	104	105	+1	1·18
	D	Gerlinde R. ..	F	27	82	82	0	0·84

Trial II

There were again three feeding groups in Trial II. The Mixtures used were B1 and B2, which were Mixture B with 12½ per cent or 25 per cent of dried skimmed milk added. The trial lasted 24 weeks at the Augustinusstift, from April 12 to September 25, 1948, and 22 weeks at the Duisburg Home, from April 24 to September 24, 1948.

The rate of weight increase of the children was about the same in all three groups (Table 35). This very satisfactory result was accompanied by a complete freedom from any sign of intolerance of the cereal and soya mixtures; the

TABLE 34

Haemoglobin values of children of from 2 to 5 years old in Trial I in the Augustinusstift

	Mixture A diet				Mixture B diet				Cow's milk diet		
		Haemoglobin percentage				Haemoglobin percentage				Haemoglobin percentage	
Name	at beginning of Trial I	at end of Trial I	alteration	Name	at beginning of Trial I	at end of Trial I	alteration	Name	at beginning of Trial I	at end of Trial I	alteration
Edeltraud ..	76	75	− 1	Walther	86	91	+ 5	Martin ..	86	76	− 10
Theodor ..	81	86	+ 5	Richard	84	80	− 4	Hans Werner	82	84	+ 2
Ute ..	75	75	0	Rose ..	78	87	+ 9	Dagmar ..	65	68	+ 3
Klaus Peter ..	78	83	+ 5	Elfrida	76	80	+ 4	Wilfrid ..	82	72	− 10
Franz Josef ..	80	81	+ 1	Rolf ..	77	90	+ 13	Reinhard ..	85	78	− 7
Augustine ..	84	80	− 4	Rudolf	79	98	+ 19	Hermann ..	—	—	
Gertrud ..	—	—		Margot	76	80	+ 4	Rudi ..	105	83	− 22
Hans Joachim	88	88	0	Volker	64	79	+ 15	Karin ..	—	—	

TABLE 35

Performance of children of from 2 to 5 years old in the Augustinusstift and in the Waisenhaus at Duisburg, expressed as change in percentage of standard body weight and as ratio of actual to standard body weight gain

Trial II

Supplementary drink	Augustinusstift (A) or Duisburg (D)	Name	Sex	Age at beginning (months)	Percentage of standard weight			Ratio of actual to standard weight gain
					at beginning	after 24 weeks	alteration	
Mixture B1	D	Ulrika G. ..	F	54	73	80	+ 7	2·50
Malted barley, wheat	D	Johannes N. ..	M	47	92	97	+ 5	2·00
and soya flour; 12½	A	Volker	M	30	81	84	+ 3	1·37
per cent dried skim-	A	Hans Werner ..	M	33	104	106	+ 2	1·33
med milk. Short	D	Wilfrid N. ..	M	46	87	88	+ 1	1·29
heating.	A	Rudi	M	30	86	87	+ 1	1·10
	A	Hans Joachim ..	M	27	88	88	0	1·00
	A	Rudolf	M	26	97	97	0	0·99
	D	Brunnhilde R. ..	F	43	90	90	0	0·95
Mixture B2	A	Klaus Peter ..	M	30	101	107	+ 6	2·00
Malted barley, wheat	D	Karl Heinz G. ..	M	42	89	93	+ 4	1·67
and soya flour; 25	D	Roswitha M. ..	F	47	72	76	+ 4	1·44
per cent dried skim-	A	Parsival	M	28	84	88	+ 4	1·41
med milk. Longer	D	Klaus M.	M	43	89	90	+ 1	1·29
heating.	A	Margot	F	28	87	90	+ 3	1·27
	A	Rose	F	40	115	116	+ 1	1·25
	D	Manfred K. ..	M	52	84	85	+ 1	1·12
	A	Dagmar	F	30	91	90	− 1	0·87
	A	Martin	M	35	94	93	− 1	0·78
	D	Marga M... ..	F	26	87	85	− 2	0·67
	D	Renate K... ..	F	53	90	88	− 2	0·50
	A	Walther	M	44	104	98	− 6	negative
Cow's milk	D	Horst M. ..	M	34	72	82	+ 10	2·58
	D	Adelheid S. ..	F	49	81	86	+ 5	1·87
	D	Ursule B. ..	F	44	99	104	+ 5	1·85
	D	Elke G. ..	M	35	83	87	+ 4	1·55
	A	Hermann ..	M	24	96	100	+ 4	1·31
	D	Hugo V. ..	M	56	90	91	+ 1	1·20
	A	Elfrida ..	F	32	102	103	+ 1	1·13
	A	Augustine ..	F	37	100	100	0	1·00
	A	Theodor ..	M	34	88	87	− 1	0·70
	A	Jürgen ..	M	28	91	89	− 2	0·62
	A	Rolf ..	M	32	95	93	− 2	0·59

TABLE 36

Performance of children of from 2 to 5 years old, for the first 8 weeks in the Augustinusstift and for 10 weeks in the Waisenhaus, Duisburg, expressed as change in percentage of standard body weight and as ratio of actual to standard body weight gain

Trial III

Supplementary drink	Augustinusstift (A) or Duisburg (D)	Name	Sex	Age at beginning (months)	Percentage of standard weight at beginning	after 8 or 10 weeks	alteration	Ratio of actual to standard weight gain
Mixture C	A	Detlef	M	30	92	97	+5	3·18
Malted barley, wheat	A	Adelheid ..	F	30	113	118	+5	3·00
and soya flour. No	D	Paul P.	M	29	100	102	+2	2·43
skimmed milk. Heat-	D	Dietrich K. ..	M	22	82	84	+2	2·00
ed to destroy trypsin	A	Volker	M	36	83	86	+3	1·94
inhibitor.	A	Annelie	F	30	106	108	+2	1·75
	A	Hermann	M	28	103	105	+2	1·75
	A	Parsival	M	34	87	89	+2	1·67
	D	Norbert N. ..	M	51	89	90	+1	1·52
	A	Martin	M	41	93	94	+1	1·48
	D	Ulrika G. ..	F	59	81	82	+1	1·43
	D	Werner D. ..	M	31	93	94	+1	1·43
	A	Marga	F	60	93	93	0	0·83
	A	Gertrud	F	32	120	118	−2	0·75
	D	Marlies T. ..	F	55	86	85	−1	0·69
	D	Elke G.	M	40	91	90	−1	0·69
	A	Luise	F	61	94	93	−1	0·67
	A	Edeltraud ..	F	71	88	81	−7	0·33
Mixture C2	D	Renate K. ..	F	58	89	96	+7	3·70
Same as above with	A	Hans Werner ..	M	39	105	110	+5	3·33
10 per cent of dried,	D	Jürgen F. ..	M	30	83	87	+4	2·57
skimmed milk.	D	Rudi B.	M	45	98	101	+3	2·29
	D	Marga M. ..	F	31	92	96	+4	2·00
	D	Ursule B. ..	F	50	103	107	+4	1·89
	D	Walther W. ..	M	25	84	86	+2	1·50
	A	Hans Joachim ..	M	34	88	89	+1	1·43
	A	Sophie	F	27	93	94	+1	1·37
	A	Klaus Peter ..	M	36	108	107	−1	0·93
	A	Willi	M	59	97	96	−1	0·50
	D	Willi H. ..	M	25	82	81	−1	0·28
	A	Margot	F	35	88	86	−2	0·02
	A	Paul Günther ..	M	37	101	99	−2	negative
	A	Adolf	M	37	81	78	−3	negative
	A	Gustav	M	52	89	86	−3	negative
Cow's milk	A	Rudolf	M	32	96	101	+5	3·34
	A	Elfrida	F	38	102	108	+6	3·32
	D	Fritz T.	M	39	84	88	+4	2·86
	A	Walther	M	51	97	101	+4	2·83
	D	Karl Heinz G. ..	M	48	92	95	+3	2·67
	D	Brunnhilde R. ..	F	48	93	96	+3	2·67
	A	Theodor	M	40	87	89	+2	2·08
	A	Simson	M	33	81	83	+2	2·00
	A	Dagmar	F	35	91	93	+2	1·94
	D	Werner D. ..	M	31	96	98	+2	1·78
	D	Ferdinand G. ..	M	32	85	87	+2	1·72
	D	Wolfgang W. ..	M	31	86	88	+2	1·72
	D	Heinz K.	M	22	76	79	+3	1·60
	A	Rolf	M	38	92	93	+1	1·60
	A	Helga	F	41	118	119	+1	1·43
	A	Horst	M	62	85	86	+1	1·17
	A	Rudi	M	36	87	87	0	0·50
	A	Kurt	M	63	100	98	−2	0·00
	D	Adelheid S. ..	F	54	88	86	−2	negative
	A	Rose	F	46	116	113	−3	negative

addition of the dried skimmed milk made a marked improvement in the taste, and even at the Augustinusstift the mixtures were drunk without complaint for nearly the whole length of the trial. Towards the end, however, one or two

of the Augustinusstift children needed some coaxing, presumably because the sweet and malty flavour had begun to cloy.

It was most unfortunate that many children were removed from the Duisburg Home before the end of the trial. The children there gained more weight, on the whole, than those at the Augustinusstift, particularly in the cow's milk group.

Trial III

In Trial III there were the usual three feeding groups. At Duisburg, the cereal and soya Mixture C and the cereal, soya and milk Mixture C2 were used for ten weeks, from September 29 to December 10, 1948. Mixture C was made of malted barley, wheat and soya flour with no skimmed milk added. It was heated long enough to destroy the trypsin inhibitor. Mixture C2 was the same but with 10 per cent of dried skimmed milk. At the Augustinusstift, the Mixtures C and C2 were used for the first eight weeks, and then, for another eight weeks, all the children were given the Mixture D2, which was like

TABLE 37

Performance of children of from 2 to 5 years old for the second 8 weeks in the Augustinusstift, expressed as change in percentage of standard body weight and as ratio of actual to standard body weight gain

Trial III

Supplementary drink	Name	Sex	Age at beginning (months)	Percentage of standard weight			Ratio of actual to standard weight gain
				at beginning	after 8 weeks	alteration	
Mixture D2	Gustav ..	M	54	86	91	+5	4·40
Malted barley,	Willi	M	61	96	99	+3	3·20
maize and soya	Adolf.. ..	M	75	78	81	+3	3·00
flour; 10 per cent	Luise	F	63	94	97	+3	2·63
dried skimmed	Edeltraud ..	F	73	81	89	+8	2·25
milk. Heated to	Parsival ..	M	86	89	91	+2	2·00
destroy trypsin	Paul Günther	M	39	99	101	+2	2·00
inhibitor.	Sophie ..	F	29	94	96	+2	1·43
	Marga ..	F	62	93	94	+1	1·33
	Martin ..	M	43	94	94	0	1·03
	Hans Werner	M	41	110	109	−1	0·80
	Gertrud ..	F	34	118	116	−2	0·75
	Annelie ..	F	34	108	106	−2	0·25
	Volker ..	M	38	86	84	−2	0·00
	Klaus Peter ..	M	38	107	105	−2	negative
	Adelheid ..	F	32	118	114	−4	negative
Cow's milk	Horst.. ..	M	64	86	90	+4	3·67
	Walther ..	M	53	101	103	+2	3·20
	Rudi	M	38	87	88	+1	1·67
	Helga ..	F	43	119	120	+1	1·29
	Rolf	M	40	93	93	0	0·80
	Rose	F	48	113	113	0	0·80
	Theodor ..	M	42	89	89	0	0·67
	Kurt	M	65	98	97	−1	0·30

Mixture C2 except that it contained maize instead of wheat flour; the con centration of the drinks was increased so that they provided 500 instead of 330 Calories a day. The control group received fresh cow's milk, providing 330 Calories, throughout.

Table 36 shows that Mixture C gave rather better weight gains than Mixture C2, but that the milk diet was again slightly the best. The response of the children was not exactly the same at the two Homes. At Duisburg there was no obvious difference between Mixtures C and C2. At the Augustinusstift the results with Mixture C2 were decidedly poor, but those with Mixture C were much better; the result was due partly to the chance that there was rather more infective illness in the group having Mixture C2. The children preferred Mixture C2 to Mixture C because it had a better taste, but with Mixture C the average daily number of stools was slightly increased. Since Mixture C2 contained milk, it should have produced better results than Mixture C, and the fact that it did not must have been due to the fault in manufacture to which reference has already been made (p. 79).

The results of the change to Mixture D2 (Table 37) were on the whole judged to be favourable, especially in those children who had previously received Mixture C2. The children took Mixture D2 with pleasure and it did not cause any gastro-intestinal upset, or any increase in the number of stools.
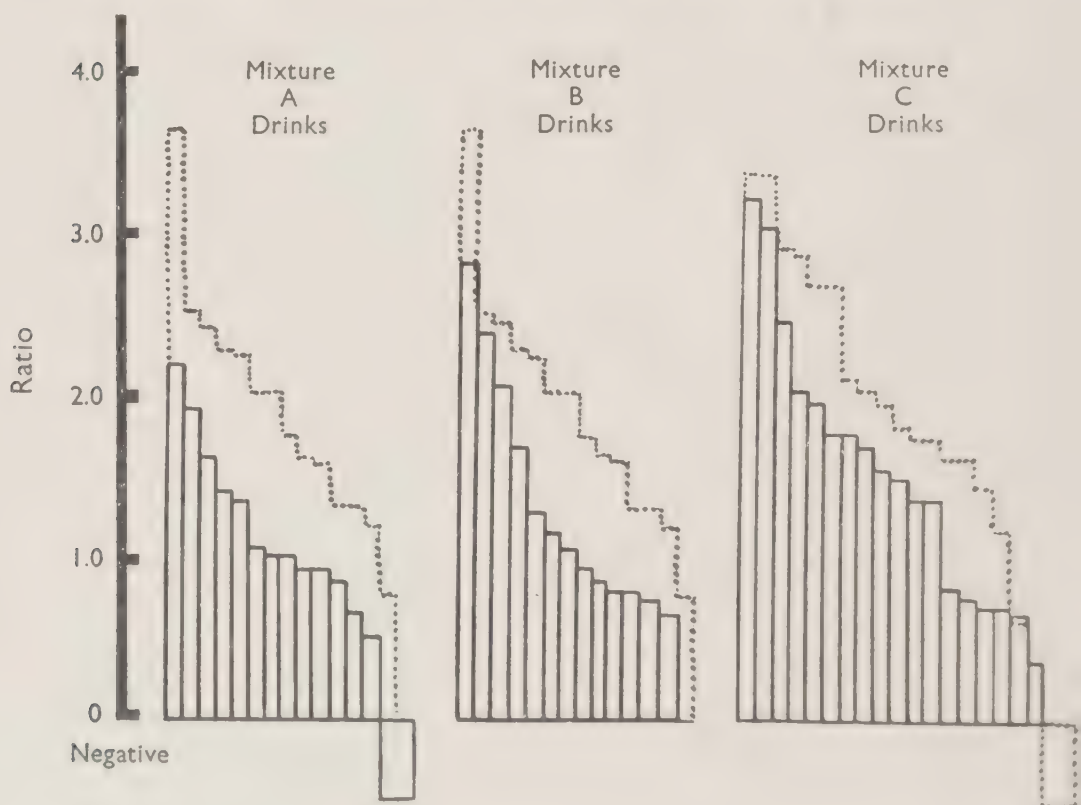
FIG. 6(a).

Ratios of actual to standard weight gains of children of from 2 to 5 years old given the cereal and soya drinks which did not contain any milk. The dotted lines indicate the ratios of the children given the cow's milk drinks.

MIXTURE A.   Malted barley, wheat and soya flour. No skimmed milk powder. Short heating.

MIXTURE B.   As Mixture A. Longer heating.

MIXTURE C.   As Mixture B. Heated to remove trypsin inhibitor.

*Summary of Trials I, II and III with Children of from 2 to 5 Years Old
in the Augustinusstift and in the Waisenhaus at Duisburg*

The contribution of 330 Calories made by the daily drinks represented between 20 and 30 per cent of the total calories supplied by the diets at both Homes.

The results of the trials, set out graphically in the same way as for the other age groups, are compared in Figs. 6(*a*) and (*b*). There was little to choose between the three milkless mixtures in their ability to assist growth. Mixture A did not cause the unfortunate effects which it caused in the younger children, and did not seem to be much inferior to Mixture B, except on the score of taste. Mixtures A and B were both surpassed by Mixture C, probably because
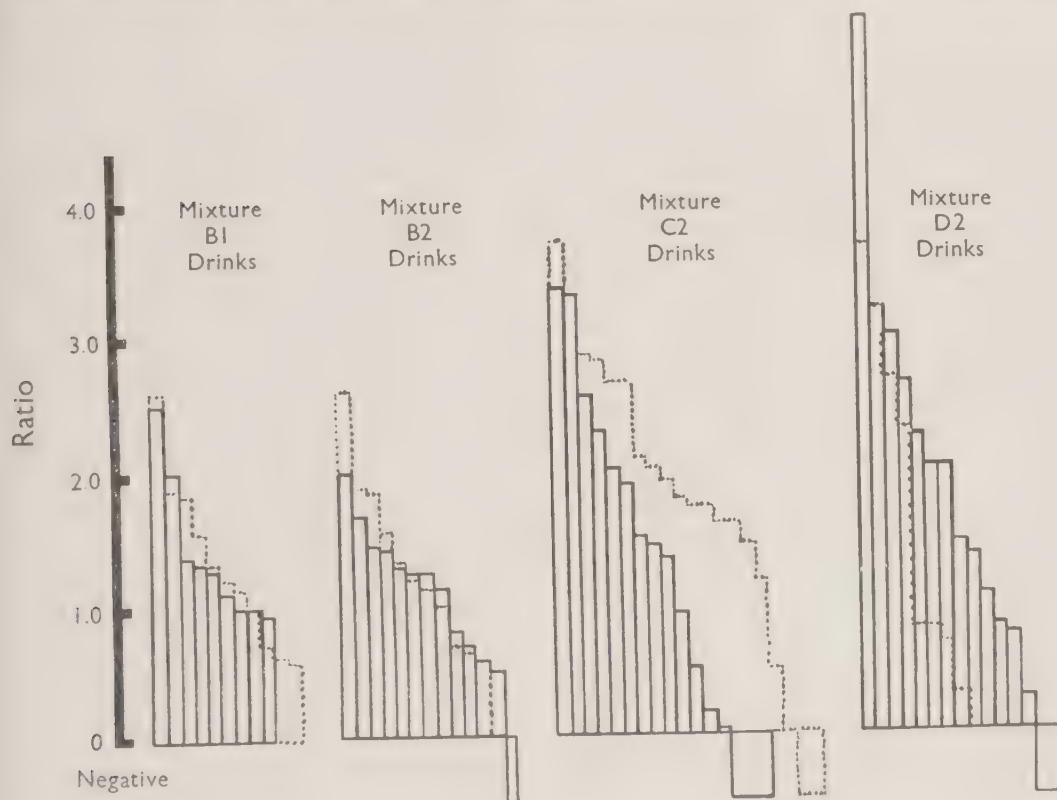
FIG. 6(*b*)

Ratios of actual to standard weight gains of children of from 2 to 5 years old given the cereal and soya mixture drinks which contained some milk. The dotted lines indicate the ratios of the children given the cow's milk drinks.

MIXTURE B1. Malted barley, wheat and soya flour. Skimmed milk powder 12½ per cent. Short heating.
MIXTURE B2. As Mixture B1. Skimmed milk 25 per cent.
MIXTURE C2. As Mixture B1 but skimmed milk solids 10 per cent. Heated to remove trypsin inhibitor.
MIXTURE D2. As Mixture C2 but with maize instead of wheat flour.

the trypsin inhibitor had been removed from the soya flour used in it. Of the other mixtures, Mixture B2, which contained the highest proportion of skimmed milk and therefore of total protein, may have been the most successful in producing weight gain, but the short trial of Mixture D1, which contained much less milk. suggested that it might have been equally good or even better. It had the advantage of tasting excellent, was almost as white as milk. and kept

very well. It had no adverse effect on the digestive tract as far as could be ascertained, and certainly deserved more extensive trial. It was one of the mixtures chosen for testing on newborn children (see p. 116).

In summary, it seems justifiable to state that in the age group 2 to 5 years old, as in the younger groups, the cereal and soya mixtures showed that they could deputize for milk to a very large extent. If they were well made, if the trypsin inhibitor was removed from the soya, and if they were combined with a little skimmed milk, they were apparently an almost complete substitute. It must be emphasized that they were supplementing diets which contained extremely little animal protein.

Trials with Schoolchildren of from 7 to 11 Years Old at Ludwigshafen-am-Rhein

THE SCHOOLS

The town of Ludwigshafen is an industrial centre on the left bank of the Rhine about 50 miles south-west of Frankfurt. It had been much damaged in the war, and contained one of the large factories of the I. G. Farbenindustrie. An explosion occurred in the factory in August, 1948, just before the feeding trial began. It caused many deaths and further damage to the town, and by its dislocation of normal life added to the difficulties of the inhabitants.

An American team of the Society of Friends was working in the town and in June 1948 members of the Medical Research Council Unit were invited to visit the team and to inspect some of the local children, who were thought to be in a poor state of nutrition. A rough survey of the children in two schools, the Goethe and Gräfenau schools, in a poor district of the town near the Friends' Settlement, showed that the children were indeed considerably undersized in comparison with English or American children of the same age, and it was decided to carry out a feeding scheme during the whole of the next school term. The upper limit of the number that could be fed was fixed at 500, and the group aged from 7 to 11 years was chosen because it would consist of children who should be growing very rapidly, but whose calorie intake would not be at the maximum, which is normally reached in later years. Any supplement given would, therefore, form a larger proportion of the total calories than it would for older children.

One of the two schools, the Goethe school, was a large, comfortless and gloomy building, two stories high. It had escaped serious damage, but the other school, the Gräfenau school, which was built on a more modern plan of separate units, was largely ruined. Many of the classes of the Gräfenau school were therefore held in the Goethe school, and at both schools, because of lack of space, a shift system was worked so that children attended morning school one week and afternoon school the next week, and so on. The times when the children could have their mid-day meal were therefore variable. Most of the children lived in the immediate vicinity of the schools, with the highest concentration around the Gräfenau school. The district was one inhabited almost exclusively by the poorer working class. Although it was crowded, because housing shortages compelled a density of about two persons to every habitable room, it had an air of desolation.

NATURE OF THE SUPPLEMENTS

No record of the complete diets could be made since the scheme was to give at school a daily supplementary meal containing the test materials.

The supplements were of four kinds, each providing 500 Calories daily. They were (1) the cereal and soya Mixture C containing malted barley, wheat and soya flour which had received some heating (see p. 58), (2) the Mixture C1 which was the same as Mixture C with 10 per cent of dried skimmed milk added, (3) full-cream dried milk, and (4) biscuits. The formula for the biscuits in parts by weight was:

> White flour 45,
> Sugar 15,
> Fat (margarine) 15.

Orange juice was served with the biscuits. The purpose of including the biscuit supplement was to provide calories with very little protein. The amount of protein provided by the supplement of Mixture C was 22·0 g., of Mixture C1 24·5 g. of which 3·0 g. was from milk, of full-cream milk 25 g., and of biscuits 6·5 g.

With each supplementary meal, each child received three tablets containing vitamins and minerals. According to the maker's analysis each tablet provided:

> Vitamin D, 500 U.S.P. units,
> Vitamin A, 5,000 U.S.P. units,
> Vitamin B_1, 1 mg.,
> Riboflavin, 2 mg.,
> Nicotinic acid, 10 mg.,
> Vitamin C, 30 mg.,
> Calcium, 375 mg.,
> Phosphorus, 250 mg.,
> Iron, 10 mg.

To assist in the scheme the Unit acquired a competent German assistant who was accepted by the Friends as a temporary member of their team; she was made responsible for the distribution of the food and the collection of the records.

METHOD OF SELECTING AND GROUPING THE CHILDREN AND OF DISTRIBUTING THE FOOD

Since the children were selected for the trial, some account of the method of selection is necessary.

The number of children of both sexes at the two schools who were aged from 7 to 11 years was about 1,100, and they were all weighed and measured on the first two days of the school term. Between 700 and 800 children were then selected for clinical examination, as being those farthest below British and American standards for weight and height. The clinical examination was made in the next few days, and each child was weighed and measured again, and the record cards (see Appendix B) were completed. The number of children finally taken for the scheme was 625, the criteria of selection being not only low weight and height for age, but also poor clinical condition. No child in whom any signs of disease could be detected was included. Only 500 of the children could be fed, but 125 further children were taken as an unfed, negative control group.

The children were grouped by the method already described (see p. 55), and a small card, coloured according to the group, was written for each child. The cards bore the Friends' stamp, and were the tickets which allowed admission to the food distribution centre. They were handed by the teachers to the

children concerned, with a leaflet addressed to the parents, explaining the scheme and enjoining regular attendance for six days a week, although there were only five school days. The leaflet is reproduced in Appendix C. It contained instructions for each child to bring a tin which would hold the food, and a spoon with which to eat it.

A large basement hall in the Gräfenau school, and two adjoining classrooms, were placed at the disposal of the Unit for the feeding scheme. The foods were prepared in the hall, and were kept until needed in large tubs which were set up at four points conveniently separated. The cereal and soya mixtures and the dried milk were made up with warm water, and their tubs had vacuum jackets which prevented too rapid cooling. Each of the four stations was staffed by two German woman-helpers recruited by the Friends.

The children were encouraged to come for the meal, not all at the same time, but at any time after 12 noon which fitted best with their school hours and home meals. When they arrived they reported to attendance clerks at a table near the door of the hall, showed their admission cards, and had their attendance recorded; children were thus prevented from presenting themselves for the same meal more than once. The clerks rapidly got to know each child, and were able to prevent the entrance of children who had been lent cards by their proper owners. The children went from the attendance clerks to the station appropriate to their feeding group, and were served from the tubs into the receptacles they had brought. They were at the same time given the vitamin tablets. They took the food to one or other of the two classrooms, and sat in a section reserved for their group, where they ate the food under supervision, which was especially needed to prevent the children who got biscuits from sharing them with other children. The biscuits were extremely popular because they were sweet and of good flavour. A child had to eat all its food before it was allowed to leave the classroom, and to ensure that it had done so an inspection was made of the empty tins which had held the liquid food, and pockets, stockings and other hiding places were searched for the biscuits.

After the first few days the various helpers and the children became accustomed to the routine, and it was possible to complete the feeding within about an hour.

RESULTS OF THE TRIAL WITH SCHOOLCHILDREN AT LUDWIGSHAFEN

The trial lasted thirteen weeks, from September 21 to December 22, 1948. There were originally 125 children in each of the groups, but in computing the results only those children were considered who attended for feeding on at least five days out of six.

The numbers of children were large, so that it was possible to compare the results obtained in the different groups by a system of "pairing". Each child in the group receiving the cow's milk was matched with a child of the same sex in each of the other groups who, at the beginning of the trial, had been similar in age, clinical status, and weight and height for age. The group having biscuits was compared with the groups having Mixture C and Mixture C1. The method counteracted the element of unreliability, inevitably introduced by comparison between groups whose composition, though equal at the beginning of the trial, had become unequal through omission of those children whose attendances had not been satisfactory. For about 14 per cent of the children the records failed to meet the criterion of attendance, so that the final analysis included 535 of the 625 originally selected (see Table 38).

TABLE 38

Number of schoolchildren in the Ludwigshafen Trial who attended less than 5 times a week to receive the food supplements

Supplement	Number who failed to attend		
	Boys	Girls	Total
Cereal and soya mixture C	24	7	31
Cereal and soya mixture C1			
including dried milk ..	16	9	25
Full-cream dried milk ..	9	8	17
Biscuits	7	10	17

The biscuits were so popular that if a child failed to come for them, it could be assumed that it was prevented by illness or by some other reason which genuinely made attendance impossible. The non-attendances in the group having biscuits could, therefore, be used as a rough measure of unavoidable absence in all four groups. From Table 38 it is seen that about seventeen children in each group were probably unavoidably absent. The excess of absences in the groups having Mixtures C and C1 was made up entirely of boys.

Mixture C was the least popular of the supplements, and a few children gave up attending altogether when they found they could not change from it to another food; others became irregular in attendance. One child, who vomited on several days about a quarter of an hour after he had drunk his Mixture C, was allowed to change to the milk group, but his record was abandoned.

The gains in weight and height are shown in Table 39, expressed as the ratio of actual increase to standard increase, and the results of comparing the means for the paired children in the various groups are given in Table 40.

TABLE 39

Mean ratio of actual increase to standard increase in height and in weight for all the schoolchildren who completed the Trial at Ludwigshafen

Sex of children	Ratio for children receiving as dietary supplement:				
	Mixture C	Mixture C1	full milk	biscuits	no addition
Weight					
Boys	1·09	1·22	1·16	0·81	0·65
Girls	1·34	1·56	1·59	1·06	0·80
All	1·25	1·40	1·35	0·94	0·73
Height					
Boys	1·35	1·35	1·21	1·26	1·12
Girls	1·12	1·25	1·34	1·22	0·81
All	1·23	1·30	1·25	1·24	0·97

TABLE 40

Comparison of mean ratios of actual increase to standard increase in weight and in height for the schoolchildren at Ludwigshafen arranged in comparable pairs according to their status at the beginning of the Trial

Supplement	Mean ratio for sets of pairs					
Weight						
Cereal and soya Mixture C ..	1·21	—	1·18	—	—	—
Cereal and soya Mixture C1	—	1·46	—	1·42	—	—
Full-cream dried milk ..	—	—	1·34	1·42	1·37	1·41
Biscuits	0·87*	0·89	—	—	0·83	—
No addition	—	—	—	—	—	0·80
Height						
Cereal and soya Mixture C ..	1·26	—	1·26	—	—	—
Cereal and soya Mixture C1	—	1·27	—	1·31	—	—
Full-cream dried milk ..	—	—	1·32	1·28	1·29	1·28
Biscuits	1·25	1·24	—	—	1·27	—
No addition	—	—	—	—	—	0·95
Number of pairs	47	49	58	57	58	62

* Each value printed in italics is significantly different from the other value in the same column ($p = {<}0·01$).

The results are printed in italics when the differences were found to be statistically significant. For boys and girls together the weight gains of the group having milk and of the two groups receiving the Mixtures C and C1 were nearly the same; the group having biscuits failed to reach the standard gain, and the control group was even worse. The weight gains of the children receiving milk or Mixture C or C1 were significantly better than those of the children who had biscuits. The amount of height gained by all the groups was about the same except in the control group, where it was significantly lower than in the others.

The weight increases of the girls were throughout better than those of the boys, but the boys usually grew better in height.

There was a considerable improvement in the general appearance of the children, even after the first month of the trial, and the improvement was maintained to the end. It was the opinion of all who watched the children that they looked fatter and better fed, and there is no doubt that the addition of 500 Calories a day made a valuable supplement to the rest of their diets. The clinical examinations at the end of the trial (Table 41) supported the common opinion, although the results did not follow exactly the results of the measurements of height and weight. The examinations indicated an increase in subcutaneous fat, and an improvement in posture. There was no decrease in the size of the thyroid gland; on the contrary, a few more children were found to have palpable enlargements and the number thus affected was about the same in all five groups, including the control group. The increase may have represented the normal change of incidence at the approach of puberty.

The town authorities of Ludwigshafen were able to arrange for large numbers of children to go away on holiday during the autumn. Most of them went to

TABLE 41

Alterations in clinical grading of the schoolchildren at Ludwigshafen between the beginning and end of the feeding trial

Supplement	Percentage of children graded:					
	at beginning of trial			at end of trial		
	A	B	C	A	B	C
Cereal and soya Mixture C ..	6	78	16	39	57	4
Cereal and soya Mixture C1	11	76	13	36	58	6
Full-cream dried cow's milk ..	17	72	11	38	52	10
Biscuits	10	76	14	31	65	4
No supplement	8	76	16	19	68	13

country districts, usually in the mountains, where the food, and the living conditions, were said to be healthy and good. The holiday, or time for recuperation (*Erholung*), lasted for from four to six weeks. The authorities agreed not to send away any of the children who were receiving supplements in the trial, but 14 boys and 22 girls in the control group had the benefit of the holiday. For these children, who were examined only at the beginning and end of the trial, and whose records are not included in the results shown in Tables 39 and 40, the ratio of actual to standard weight increase was 1·08 for the boys and 0·84 for the girls; the ratio for height was 1·28 for the boys and 0·71 for the girls. Compared with the children who stayed at home and were not fed in the trial, the boys gained slightly more in weight and height but the girls were not much affected.

In all the groups receiving the extra food, the gains were greatest at the beginning of the trial and decreased towards the end. For all children, including those who did not take part in the whole trial, the average gain of weight in the first month was 2·2 times greater than the standard gain. In the next month it was only 1·4 times as great, and in the third month only 0·8. All groups participated in this decline, for which there was no obvious explanation. Although there had been such considerable increases in weight, the children were still, on an average, only 95 per cent of the standard weight at the end of the trial.

CONCLUSION

The trial with the Ludwigshafen schoolchildren demonstrated that, as a supplement supplying an additional 500 Calories daily, cereal and soya mixtures, with or without 10 per cent of dried skimmed milk, were as effective as full-cream dried milk in restoring the weight and height of undernourished children, and were superior to a calorie equivalent of biscuits.

Trials with Newborn Children in the Landesfrauenklinik

THE INSTITUTION

The Landesfrauenklinik was a large modern hospital under the direction of Professor K. J. Anselmino. It had escaped damage in the war, and was well run and fully staffed. In its maternity department about 200 children were born each month. Every child was weighed before and after each feed, and the records of diet and progress were carefully and accurately kept.

Most of the infants available for study were those who had been born in the hospital, and would normally leave at the end of ten days. A few were those who were kept longer because of the illness or delayed recovery of the mother, and a few had been readmitted with their mothers for various reasons. Only those babies could be included in the trial whose mother's milk was inadequate or had failed completely. The numbers were therefore small, but they provided useful if limited information about the reaction to the cereal and soya mixtures in the first weeks of life.

The Original Diets

As has just been explained, the infants available for study in the Landesfrauen-klinik were those who could not be fed by their mothers. There was always some human milk to be had in the hospital, but not enough for all those who needed supplementary feeding; premature infants and others considered to be especially in need of human milk were given priority. Artificial foods based on dried cow's milk, such as are commonly used for feeding infants in England, were not used in the hospital, and seemed never to have been popular in Germany. The substitute for breast milk always employed was fresh cow's milk, diluted with water and fortified with sucrose. The milk was well boiled, and the hospital's standard of cleanliness in feeding operations was high.

Diets used in the Trials

The cereal, soya and milk Mixtures D1 and D2 were those used to replace some of the cow's milk in the babies' diets. They contained malted barley, maize and soya flour, with 10 per cent of skimmed milk solids. They had been subjected to heating which destroyed the trypsin inhibitor completely. Mixtures D1 and D2 were the same except that the latter was made on the larger scale.

The plan usually followed was to replace at first one of the usual bottle feeds of milk by a bottle feed of the mixture. A careful watch was kept for signs of intolerance, and if after a few days no such signs appeared, another milk feed was replaced, and so on until about half the total calories was being obtained from the mixture; the proportion of one half was not often exceeded, though there were some exceptions among the older infants.

The mixture feeds were made by stirring 150 g. of the dry powder into a little cold water, adding hot water to make up to one litre, and boiling for a few minutes. The feeds were always given at once. Their content of 600 Calories per litre was the same as that of the sweetened cow's milk they were replacing, and they were used in the same way as the milk. They flowed easily through the ordinary bottle teat, but when they had cooled, needed to be shaken a few times to prevent sedimentation. They were taken readily by the infants, who seemed to like the sweet and agreeable taste.

The babies remained under the care of their usual nurses and doctors. A member of the staff of the Hospital was seconded to the Unit and it was his duty to supervise the feeding of the children and to make the necessary extracts from the Hospital's records.

RESULTS OBTAINED WITH NEWBORN CHILDREN IN THE LANDESFRAUENKLINIK

The weight records of infants in the Landesfrauenklinik are given in the form of charts (Figs. 7(a), (b), (c)) in which the contribution of the experimental mixtures to the total diets is shown as the percentage of total calories.
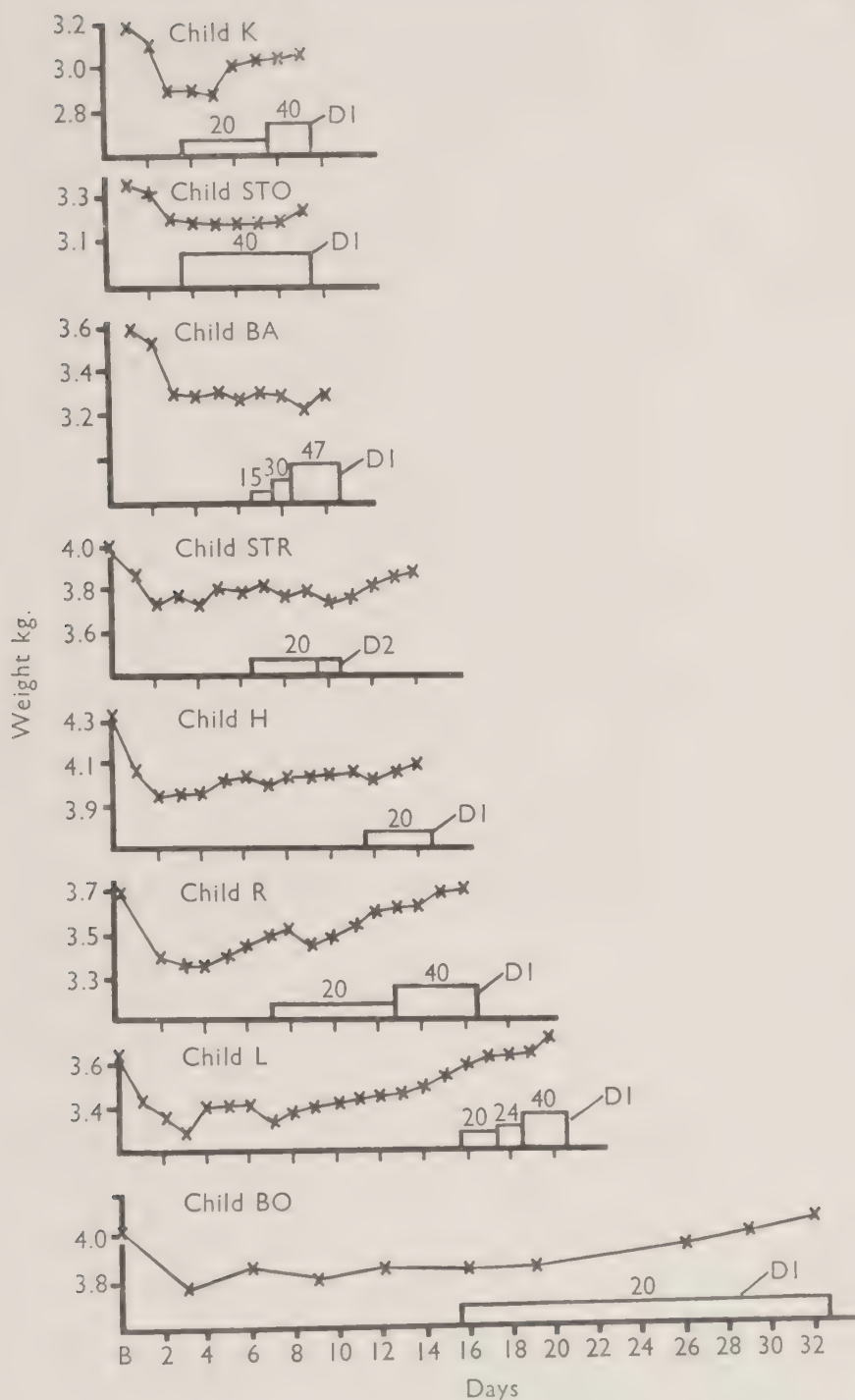
FIG. 7(a).

Infants in the first month. Only one child (STR) was given Mixture D2. He regurgitated it regularly, and did not put on weight satisfactorily. All the other children received Mixture D1, and up to 40 per cent was well tolerated, although one child (R) had slightly loose stools. The weight gains were on the whole best in the oldest children. The figures above the boxes on the diagrams show the percentage of the total calories derived from the cereal, soya and milk Mixtures D1 and D2.

Mixture D1 was apparently perfectly tolerated when it provided up to about half the total calories. This percentage was exceeded in the diets of some of the older babies, one of whom had a diet containing 80 per cent of Mixture D1 for three weeks before showing any signs of intolerance. The weight gains of the youngest infants were not very rapid, but those of the older children were excellent.

Mixture D2 was less satisfactory. The one infant given it in the first week of life regurgitated his feeds repeatedly, and the older children, although their weight gains were good for a time, all developed loose stools which did not improve until the percentage of the mixture in the diets was considerably
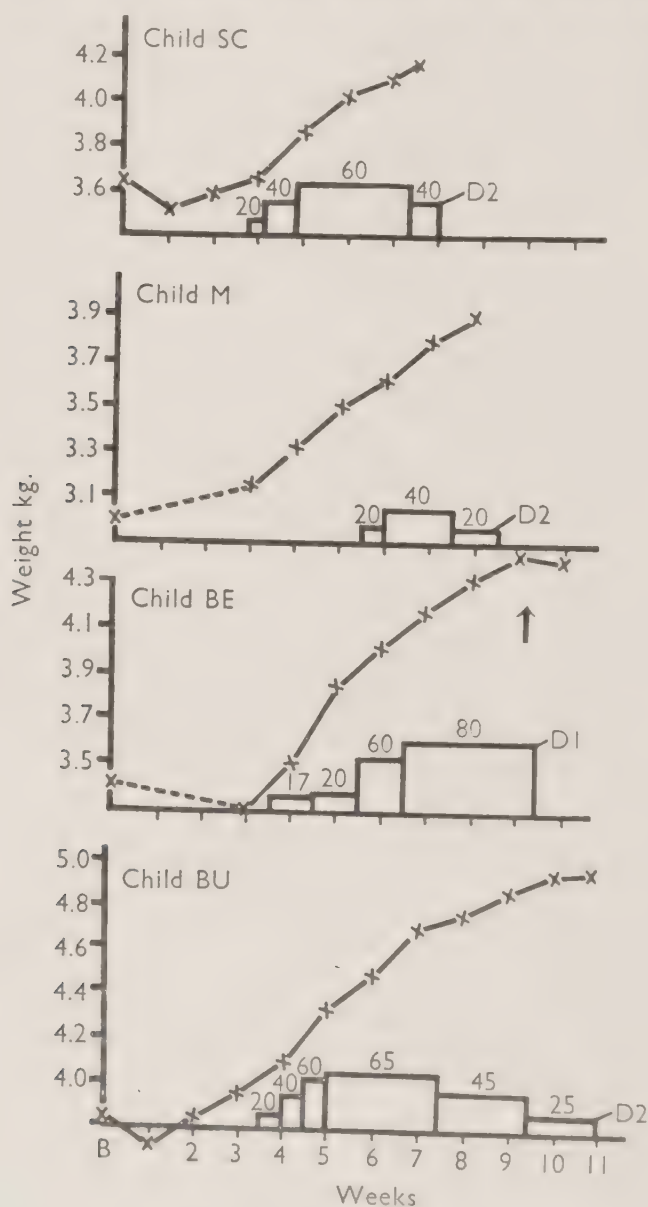
FIG. 7(b).

Infants of from 3 to 11 weeks old. The three children (SC, M and BU) given Mixture D2 all had unduly loose stools, which did not improve until the percentage of the mixture was dropped to about 20. Mixture D1 was better tolerated: the child BE had 80 per cent of it for 3 weeks, but then had a mild digestive upset. The figures above the boxes on the diagrams show the percentage of the total calories derived from the cereal, soya and milk Mixtures D1 and D2.
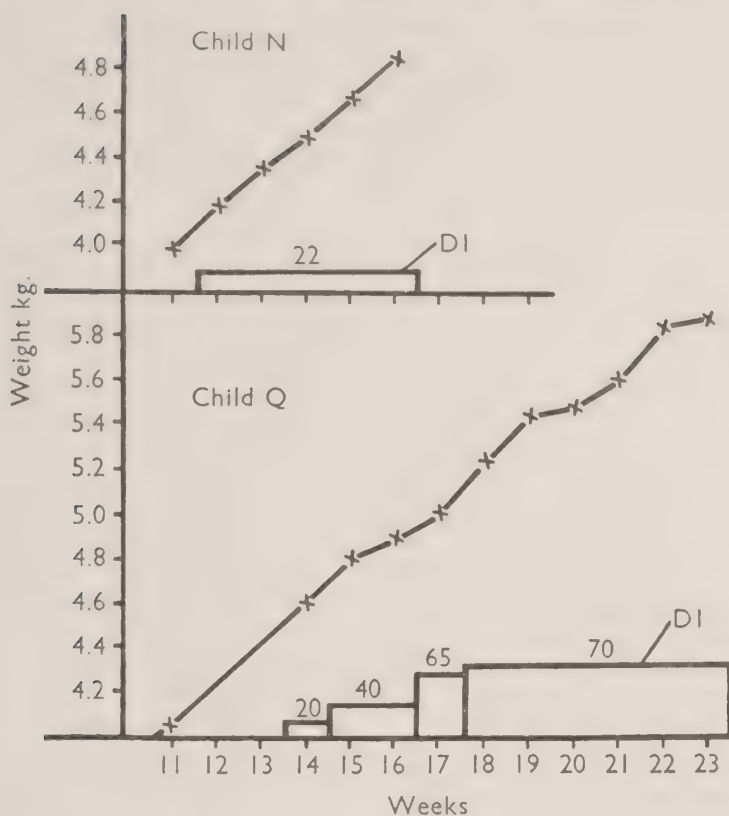
FIG. 7(c).

Infants of 11 weeks old given the cereal, soya and milk Mixture D1. The weight gains were good. The figures above the boxes on the diagrams show the percentage of the total calories derived from the cereal, soya and milk Mixture D1.

reduced. There was presumably some fault in Mixture D2 which was the result of large-scale manufacture. The failure was unfortunate, but the results of using Mixture D1 showed that if it was well made, it could replace a considerable amount of the milk even in the diets of very young children.

Discussion of Some Aspects of the Cereal and Soya Mixtures and their Use

THE AMINO-ACID COMPOSITION OF THE DIETS

On theoretical grounds, some of the mixtures, and especially Mixture A, could be criticized for shortage of some of the essential amino-acids (see Table 17, p. 62), but when the mixtures were combined with fresh milk as in the diets of the children of from 6 to 12 months old (see Table 42), these deficiencies were largely removed. All the cereal and soya diets used for this age group had a composition similar to that of the cow's milk diet, as far as the amounts of the twelve essential amino-acids determined by Block and Mitchell (1946–7) were concerned. The cow's milk diet had, however, a slightly higher proportion of its total N in the form of the twelve amino-acids. It would seem, therefore, that differences in the proportions of the amino-acids could not have been an important cause of differences in the response of the children of from 6 to 12 months old.

TABLE 42

Sources of protein and amounts of 12 essential amino-acids present in the whole diets used for children of from 6 months to 2 years old in the present investigation, and in human and cow's milk, determined by calculation from the tables of Block and Mitchell (1946–7)

(All values for amino-acids are in g. per 16·0 g. N.)

Percentage of total protein derived from different sources in the diets of:

Source of protein	children 6 to 12 months old						children 1 to 2 years old							
	Mixture A diet	Mixture B diet	Mixture B2 diet	Mixture C2 diet	Mixture D1 diet	Cow's milk diet	Mixture A diet	Mixture B diet	Mixture C diet	Mixture B1 diet	Mixture B2 diet	Mixture C2 diet	Mixture D1 diet	Cow's milk diet
Cereal and soya mixture	33	40	44	61	56	0	52	67	73	54	48	64	58	0
Milk*	29	29	39	31	25	63	0	0	0	14	28	12	9	59
Semolina or bread	38	31	17	8	19	37	48	33	27	32	24	24	33	41

Content of amino-acids in above diets (g. per 16·0 g.N) and **Content of amino-acids (g. per 16·0 g.N) in:**

Amino-acid	Mixture A diet	Mixture B diet	Mixture B2 diet	Mixture C2 diet	Mixture D1 diet	Cow's milk diet	Mixture A diet	Mixture B diet	Mixture C diet	Mixture B1 diet	Mixture B2 diet	Mixture C2 diet	Mixture D1 diet	Cow's milk diet	human milk	cow's milk
Arginine	4·5	5·0	5·2	5·6	5·0	4·1	4·7	5·4	5·6	5·3	5·4	5·6	5·4	4·2	3·7	4·3
Histidine	2·2	2·3	2·3	2·3	2·3	2·5	2·1	2·2	2·2	2·2	2·3	2·2	2·2	2·4	2·7	2·6
Lysine	4·5	4·9	5·6	5·7	5·1	5·5	3·4	4·2	4·4	4·5	5·3	4·8	4·3	5·6	6·5	7·5
Tyrosine	4·3	4·4	4·5	5·0	4·5	4·7	3·9	4·0	4·0	4·2	5·1	4·1	4·2	5·0	5·1	5·3
Tryptophan	1·2	1·3	1·3	1·3	1·2	1·4	1·1	1·1	1·1	1·2	1·3	1·2	1·1	1·4	1·5	1·6
Phenylalanine	5·6	5·6	5·6	5·7	5·6	5·6	5·6	5·6	5·6	5·6	5·7	5·6	5·6	5·7	5·3	5·7
Cystine	1·6	1·6	1·5	1·5	1·6	1·3	1·8	1·8	1·8	1·7	1·6	1·7	1·7	1·3	1·4	1·0
Methionine	2·1	2·2	2·4	2·3	2·3	2·7	1·5	1·7	1·7	2·0	2·4	1·9	2·0	3·0	2·3	3·4
Threonine	3·5	3·6	3·8	3·9	3·8	3·8	3·1	3·4	3·5	3·5	3·9	3·6	3·5	3·8	4·5	4·5
Leucine	8·3	8·2	8·6	8·1	9·1	10·0	6·9	6·9	6·8	7·6	8·1	7·4	8·5	9·6	8·1	11·3
Isoleucine	5·3	5·4	5·9	5·7	5·3	6·7	4·0	4·2	4·3	4·8	5·4	4·8	4·6	6·5	5·5	8·5
Valine	5·6	5·5	5·9	5·6	5·4	6·9	4·4	4·3	4·3	4·9	5·6	4·8	4·7	6·9	5·8	8·4
Percentage of total calories as protein in diet	12	15	18	18	16	14	9	13	13	14	16	15	14	11		

* Includes milk added to, or incorporated in, the basic cereal and soya mixtures.

The cereal and soya diets of the children of from 1 to 2 years old, except the diet with Mixture B2, contained such small amounts of milk that the theoretical deficiencies of amino-acids were not remedied, and Table 42 shows that the proportions of several amino-acids in the diets were rather low; the Mixture A diet particularly had a very small amount of lysine. All the other diets, with a few unimportant exceptions, had about the same proportions of the twelve amino-acids.

The amounts of the twelve amino-acids in human milk and cow's milk are included in Table 42 for comparison.

The various diets did not have equal amounts of total protein and the amounts of the twelve essential amino-acids supplied by 100 g. of the whole diet have therefore been calculated (Table 43). The theoretical inferiorities again appear, especially in the Mixture A diets, but it is necessary to recall that the Mixture A diet of the children of from 6 to 12 months old gave excellent results, whereas that of the children of from 1 to 2 years old gave poor results. It seems justifiable to conclude that the amounts of amino-acids present were adequate for the younger children. The smaller amounts in the diet of the older children may, on the other hand, have been inadequate and it is not surprising that when they were given Mixture A, which had also the unfortunate tendency to produce loose stools, the results were unsatisfactory. The fresh whole milk added to the diets of the younger children presumably protected them from digestive upsets.

All the other cereal and soya diets used for the children of both age groups supplied about the same amounts of the twelve essential amino-acids per 100 g. diet as the corresponding milk diets. The Mixture B2 diet of the children of from 1 to 2 years old was relatively rich in all the amino-acids, chiefly because it contained so much milk. The Mixture B diet, which gave very good results too, though it contained no milk at all, was not quite as rich and was, perhaps, a little short of leucine, isoleucine and valine. No notable alteration in amino-acid composition seems to have been made by the inclusion of maize in Mixture D1. If there had been no milk in the mixture the tryptophan might, however, have been rather low.

The average calorie intakes per kg. body weight were known, so it was possible to calculate the amounts of the amino-acids taken per kg. body weight. The results for four of the most successful cereal and soya diets are shown in Table 44. They provide some idea of the requirements of children in the age groups, 6 to 12 months and 1 to 2 years, when fed on mixed diets. Some comparable figures for tryptophan, phenylalanine, the sulphur-containing amino-acids and isoleucine for children in the first months of life were obtained by Albanese and his co-workers (see p. 10). They were, respectively, 30, 170, 100 and 90 mg. per kg.; the first three are fairly close to the values given in Table 44 for the children of from 6 to 12 months old, but the value for iso-leucine is much higher than that given by Albanese and is probably far above the minimum requirement.

THE TOTAL PROTEIN CONTENT OF THE DIETS AND FACTORS WHICH MAY HAVE CAUSED WASTE OF IT

Table 42 shows the large contributions to the total protein in the diets which were made by the cereal and soya mixtures. In the group from 6 to 12 months old, the amount of protein derived from the mixtures was always greater than the amount derived from milk, and in the group from 1 to 2 years old, milk

TABLE 43

Amounts of 12 essential amino-acids in the whole diets eaten by children of from 6 months to 2 years old determined by calculation from the Tables of Block and Mitchell (1946–7)

Amount of amino-acid in diets eaten by:

Amino-acid	children 6 to 12 months old (g. per 100 g. diet)						children 1 to 2 years old (g. per 100 g. diet)							
	Mixture A diet	Mixture B diet	Mixture B2 diet	Mixture C2 diet	Mixture D1 diet	Cow's milk diet	Mixture A diet	Mixture B diet	Mixture C diet	Mixture B1 diet	Mixture B2 diet	Mixture C2 diet	Mixture D1 diet	Cow's milk diet
Arginine	0·54	0·75	0·94	1·01	0·80	0·57	0·42	0·70	0·73	0·74	0·87	0·84	0·76	0·46
Histidine	0·26	0·34	0·41	0·43	0·37	0·35	0·19	0·29	0·29	0·31	0·37	0·33	0·31	0·26
Lysine	0·54	0·73	1·01	1·03	0·82	0·77	0·31	0·55	0·57	0·63	0·85	0·72	0·60	0·62
Tyrosine	0·52	0·66	0·81	0·90	0·72	0·66	0·35	0·52	0·52	0·59	0·82	0·62	0·59	0·55
Tryptophan	0·14	0·19	0·23	0·23	0·19	0·20	0·10	0·14	0·14	0·17	0·21	0·18	0·15	0·15
Phenylalanine	0·67	0·82	1·01	1·03	0·90	0·78	0·51	0·73	0·73	0·78	0·91	0·84	0·78	0·63
Cystine	0·19	0·24	0·27	0·27	0·26	0·18	0·16	0·23	0·23	0·24	0·26	0·25	0·24	0·14
Methionine	0·25	0·33	0·43	0·41	0·37	0·38	0·14	0·22	0·22	0·28	0·38	0·28	0·28	0·33
Threonine	0·42	0·52	0·68	0·70	0·61	0·53	0·28	0·44	0·45	0·49	0·62	0·53	0·49	0·44
Leucine	1·00	1·23	1·54	1·46	1·46	1·40	0·62	0·90	0·88	1·06	1·30	1·11	1·19	1·06
Isoleucine	0·63	0·81	1·06	1·03	0·85	0·94	0·36	0·55	0·56	0·67	0·86	0·72	0·64	0·71
Valine	0·67	0·82	1·06	1·01	0·86	0·97	0·40	0·56	0·56	0·69	0·90	0·72	0·66	0·76
Percentage of total N accounted for by the 12 amino-acids	49	50	53	53	51	55	42	45	45	47	52	48	48	56

Where the value for any amino-acid is less than 75 per cent of the amount in the corresponding cow's milk diet it has been italicized.

TABLE 44

Amounts of 12 essential amino-acids calculated from the Tables of Block and Mitchell (1946–7) and of total protein taken daily per kg. body weight by children of from 6 to 12 months and from 1 to 2 years old

| Amino-acid | Amounts of amino-acids taken daily by children from: | | | |
| | 6 to 12 months old | | 1 to 2 years old | |
	Mixture A (mg./kg. body weight)	Mixture B (mg./kg. body weight)	Mixture B (mg./kg. body weight)	Mixture B2 (mg./kg. body weight)
Arginine	144	180	194	222
Histidine	70	83	79	94
Lysine	144	176	151	217
Tyrosine	138	158	144	209
Tryptophan	38	47	40	53
Phenylalanine	180	202	202	233
Cystine	51	58	65	65
Methionine	67	79	61	98
Threonine	112	130	122	160
Leucine	265	295	248	332
Isoleucine	170	194	152	221
Valine	179	198	155	230
Total protein consumed (g. per kg. body weight daily)	3·2	3·6	3·6	4·1

provided only a small amount or none at all. For the diets of the newborn infants see p. 116. The replacement of 50 per cent of their calories by Mixture D1 involved replacing about one third of their total protein.

The amounts of total protein taken per kg. body weight with four of the most successful cereal and soya mixtures are included in Table 44. The diets of British children of from 1 to 2 years old analysed by Widdowson (1947, Table 1) contained from 3·2 to 3·7 g. total protein per kg. body weight daily. The corresponding figures for children of the same age in Table 44 are 3·6 and 4·1.

About 13 per cent of the total calories in the diets of Widdowson's children were derived from protein; in the present series the total protein in the cereal and soya diets was usually 13 per cent or a little more (Table 42), but it was only 11 per cent in the milk diet. Widdowson's children had 70 per cent of their total protein from animal sources, and milk provided three fifths of the 70 per cent. From Table 42 it is seen that the 28 per cent of animal protein, all from milk, included in the Mixture B2 diet was the greatest proportion of animal protein in any of the cereal and soya diets of the children from 1 to 2 years old, and even the milk diet had only 59 per cent of animal (milk) protein.

The assessment of the value of the protein of the mixtures would have been much more complete if it had been possible to carry out laboratory estimations of the amounts of the amino-acids. Ideally, studies should have been made also of the amino-acid and nitrogen utilization by a few children from each of the various feeding groups. The theoretical difficulties known to be inherent

in such studies are considerable (see p. 8), and the practical difficulties particularly in the group aged from 1 to 2 years, are obvious to anyone who has had the management of small children. If such experiments are carried out they should be planned so that the particular amino-acids under investigation are supplied and used in the most natural manner; the response of a child to a dose of a synthetic amino-acid, given after a period of abnormal diet lacking the acid, is almost certainly different from the response to the same amount of the acid in, for example, a milk diet given continuously.

The fact that the cereal and soya diets, despite their higher percentages of total protein, were not consistently superior to the milk diets, suggested some waste of protein, or a partial deficiency which could be made up only by an increase in the total amount of protein used. If the calculated values for amino-acid content can be accepted, the former is the more likely explanation, and it is necessary to consider how the waste may have occurred.

The Trypsin Inhibitor

Some of the experiments recorded in the literature in which a high intake of total protein was found necessary for satisfactory growth were made with soya, and the explanation which most quickly comes to mind is that the trypsin inhibitor may have been responsible. When it is present, it interferes with the use of all the protein in the diet, not merely that in the soya (see Appendix D). In the present series of trials, the inhibitor was removed from the soya used in some of the mixtures, and the results obtained with the children suggested that the removal brought about an improvement in nutritive value. It is obvious, however, that further experiments are needed before the importance of the inhibitor in child feeding can be properly established.

Variation in the Composition of the Dietary Materials

The absence of complete consistency in the results may have been due to several other factors. In the conditions prevailing in Germany at the time, it was impossible to insist on uniformity in the raw materials; the degree to which they differed from one batch to another is unknown, and may certainly have caused some variation in the proportions of amino-acids present in the finished products (see p. 12).

Damage to the Nutritive Value of the Protein

There may, too, have been modifications of the nature of the protein caused during manufacture by the "amino sugar reaction" (see p. 16). The proteins of the mixtures were constantly in contact with large quantities of reducing sugars and, in the imperfectly controlled conditions of temperature and humidity inside the large-scale drying tower, there may have been opportunities for the combination of protein or amino-acids with the sugars. The reaction can also occur spontaneously, and proceeds much more rapidly and completely if the humidity is high than if it is low. No special precautions were taken to ensure that the spray-dried mixtures remained free from moisture; it was known that they took up moisture from the air, but the possible consequences were not suspected, and further damage to the protein may have occurred during storage. The rate of change in the amino-acids in such mixtures should be measured under various conditions of temperature and humidity. The weight gains of the children in the present series of trials were not sufficiently steady to provide any evidence of change in food value with length of storage of the mixtures.

Occurrence of Loose Stools

Some of the waste of protein may have resulted from hurry through the gut, as shown by the loose stools of some of the children. Part of the trouble may have been caused by overheating during manufacture, not of the protein, but of the carbohydrate. It was noticed repeatedly that those mixtures which caused the most trouble in the young children, and also in young dogs (see p. 52), were those which had the darkest colour. The dark mixtures had almost certainly been overheated. The maximum temperature reached probably did not exceed 80° C., at which it would not ordinarily be expected that much caramelization would occur, but, in the presence of such salts as the mixtures contained, the production of caramel may have been encouraged (Bell, 1950). The caramel, or some other form of altered carbohydrate, may have had an abrasive action or been responsible in some other way for irritation of the gut.

It was at one time thought that the tendency of the mixtures, when given in large amounts, to cause loose stools might have been the result of the presence of the trypsin inhibitor. It was a disappointment to find that Mixtures C and C2, neither of which contained the inhibitor, had in less degree the same fault as Mixture A, which had to be abandoned because of the digestive upsets it caused. The trouble was probably due more to the carbohydrate of the mixtures than to the protein.

The fact that some children were affected severely, and others not at all, suggested the possibility that variation in the amounts of the digestive enzymes may have determined the reaction of the individual. The chief sugar which was present in the mixtures after malting was of course maltose. It has been used for many years, especially in Continental practice, for the relief of constipation, and there is no doubt of its laxative properties. It is a matter of common experience that different children (and adults) express very different views on the palatability of malted foods; they are liked by the majority but are disliked intensely by many people, and it is not impossible that such dislikes have a physiological basis. The ability to deal successfully with large amounts of maltose may depend on the possession of a correspondingly large amount of the enzyme maltase, but there may be other causes for failure to digest the sugar. The child Barnabas (p. 87), who ate the Mixture B2 diet with apparent pleasure, nevertheless vomited regularly about half an hour later, and one of the Ludwigshafen schoolchildren was similarly affected about a quarter of an hour after taking Mixture C (p. 113). The shortness of the time interval suggests a gastric rather than a duodenal or intestinal irritation, and it may be that the maltose had an irritant effect on the gastric mucosa. The dilution of the sugar in the stomach may have been excessive, or the mechanism which regulates the passage of sugar into the duodenum may have been faulty (Jones, 1951).

If the maltose was responsible for the gastro-intestinal upsets, it would not have been the first time that such trouble had been experienced. The critics of Liebig (p. 35) complained that his malted materials caused vomiting and diarrhoea, and the discrepancy between their results and his may have been connected with small differences in the management of the malting process which, it is now known (p. 36), can cause large differences in the proportions of the different sugars finally obtained. It is, however, apparently held in some circles even today that malted cereals are unsuitable for children less than 3 months old (Lesné, Hesse and Augerau, 1950).

In summary, it may be said that the evidence is more in favour of the defect which caused loose stools being in the carbohydrate of the mixtures than in the protein.

THE FAT OF THE DIET

The diets containing the mixtures had much less fat than the control diets, which contained full-cream cow's milk. The fat of the mixtures was nearly all derived from soya; it contains a high proportion of unsaturated fatty acids, which are possibly indispensable in human nutrition, although this is uncertain. Soya fat is said to be well absorbed and well tolerated. It can hardly have been responsible for any of the gastro-intestinal upsets, which were most severe when Mixture A was given, although it contained the smallest amount of soya. Fat did not appear to have any important part in the diet, and it would have been valuable to repeat the trials with soya from which the fat had been extracted.

THE MINERALS, VITAMINS AND GROWTH FACTORS IN THE DIET

The fortification of the mixtures with calcium should have ensured that each child received well over 1 g. of it daily, although, since no balance studies could be made, the amount absorbed was uncertain. It is known that the calcium of soya is well absorbed (p. 27), and that the amount of phytic acid is fairly low. Vitamin D was supplied in amounts which were probably well in excess of the physiological requirements, and the fact that the skeletal development of the children was satisfactory may have been evidence that the utilization of calcium was good.

Vitamins A and C also were supplied liberally. There was no evidence of shortage of any of the vitamins of the B complex, and no supplements of them were given. Probably the amounts in the mixtures were sufficient for the main-tenance and growth of the children, just as they were found adequate for rats by Chick and Slack (1946). It is not possible to say if the amounts would have been great enough to cure any existing deficiency, and the point could only be decided by actual trial.

It is perhaps even more urgent to decide whether the diets which contained no milk, or small quantities of milk, were lacking in vitamin B_{12}, or in any of the so-called growth factors (p. 22). Rat experiments (Appendix E) seemed to show that injection of vitamin B_{12} increased the appetite and weight gain of rats given Mixture B, but at the time when the trials with the children were made, vitamin B_{12} was not yet available. The danger of drawing false analogies from rat experiments is easily appreciated, but a repetition of the trials with diets including, or supplemented by, "animal-protein factor" is obviously desirable.

THE METHOD OF MANUFACTURING THE MIXTURES

More consistent results might have been obtained if the conditions of manu-facture and storage of the mixtures could have been strictly standardized. It was, for instance, almost certain that Mixture B, as supplied for Trial II, was not exactly the same as when supplied for Trial I, and Mixture D2 was not the same as Mixture D1. It is obvious that more research is needed before the best conditions of manufacture can be fully established. It is well known that the transition from the laboratory scale of manufacture to the full com-mercial scale often involves difficulties that can be solved only by trial and error, and the interposition of a pilot plant would probably have been of great help.

Cow's milk and soya undoubtedly exert special influence in mixtures by the nature of their physico-chemical properties, and the results of their influence

are seen in manufacturing processes as well as in the process of digestion. For instance, it was noticed that when a very small amount of fresh skimmed milk was added to the cereal and soya suspension before spray-drying, the character of the final powder was invariably altered (see p. 60). The beneficial effect on digestibility which was always seen when children were given fresh milk with the cereal and soya mixtures may also have had a physical or physico-chemical basis.

Conclusions

GENERAL

The trials set out to assess the value of the cereal and soya mixtures, in comparison with fresh cow's milk, by answering the three questions, whether it was possible to feed young children successfully on diets in which there was no milk or other animal protein, whether the addition of dried skimmed milk to the cereal and soya mixtures was an advantage, and whether, if the trypsin inhibitor was removed from the soya, the milk could be omitted or reduced in amount. The questions were not answered completely, but so much information was gained of a nature likely to be helpful in any future attack on the main problem that it was decided to report in full the comparative failures as well as the successes.

The most definite answer was that obtained to the first question and in the first trial. The children of from 1 to 2 years old in Trial I, who were given Mixture B, grew extremely well, and were brought into good clinical condition, although they had no milk at all for sixteen weeks. The addition of $12\frac{1}{2}$ per cent dried skimmed milk in Trial II did not seem to confer any benefit, and it was not until 25 per cent of the milk was added in Mixture B2 that greater progress was observed. The diet containing Mixture B2 had a high content of total protein, and this may have been a factor which contributed to its success.

The value of removing the trypsin inhibitor from the soya was not completely settled by the use of Mixtures of the type of C and D, because they were unfortunately deprived of some of their nutritive value by faults in manufacture. It did seem, however, that the removal was beneficial, because the addition of 10 per cent of skimmed milk to the best of these mixtures was probably as valuable as the addition of 25 per cent to Mixture B2, in which the trypsin inhibitor was still present. More tests are needed before the best method of adding milk to such mixtures can be decided. The avoidance of overheating in manufacture is of importance. The bad effects of faulty preparation were shown by the children, especially those given Mixture C2, and by the rats (Appendix E).

In Mixtures of types A, B and C the amino-acids were derived from barley, wheat and soya. In Mixture D the wheat was replaced by maize without causing any obvious alteration in quality. Under the conditions of the trials, the amino-acid composition of the mixtures may have been less important than the form in which the carbohydrate was offered.

CHILDREN UNDER 1 YEAR

When Mixture D was used in feeding the newborn children at the Landesfrauenklinik, it seemed that it could safely be given as long as it supplied up to about 40 or 50 per cent of the total calories. A further increase in the percentage sometimes produced an alteration of the stools and a reduction

in the weight gains. The children of from 6 to 12 months old in Trial I, however, who had about 35 per cent of their calories in the form of the cereal and soya Mixtures A and B, showed no signs of intolerance and throve excellently. These children had the mixtures as *Brei*, but always with an equal amount of *Brei* made with fresh cow's milk, and the milk supplied about 20 per cent of the total calories. In a subsequent Trial (III) in which the cereal and soya mixtures were not satisfactory, the fresh milk *Brei* was again found valuable in combination with cereal and soya *Brei*, and seemed to have a protective action in addition to its nutritive value. The dried skimmed milk which was included in Mixture B2 was not as effective, and it was clear that the fresh milk, which was the only new item brought by the addition of the milk *Brei*, must be the ingredient responsible for the improvement. It was not possible, however, to point to any particular virtue. The attempts made to increase the percentage of cereal and soya mixture in the diets to a figure higher than 35 were only partly successful, perhaps because the amount of milk given, and therefore the amount of some essential ingredient conveyed by the milk, was too small. The cow's milk diet, which was used as a control, derived 44 per cent of its calories from fresh milk.

CHILDREN OF FROM 1 TO 2 YEARS OLD

As mentioned above, the greatest measure of success was obtained with the children between 1 and 2 years old. The proportion of the calories supplied by the cereal and soya mixtures was between 40 and 50 per cent. The proportion exceeded that of 33 per cent supplied by the milk of the control diets. The excess was deliberate. It was one of the objects of the trials to determine the approximate limit of usefulness of the mixtures.

OLDER CHILDREN

It is usually agreed that if a child can be given about 500 g. fresh cow's milk a day, as a supplement to a fairly adequate mixed diet, it will thrive, and the provision of such an amount is often held to be a universal desideratum. The satisfactory results, therefore, obtained when the Augustinusstift and Duisburg children of from 2 to 5 years old were given 500 g. fresh milk, or its caloric equivalent of one or other of the cereal and soya mixtures, should be of immediate practical value in child-feeding schemes. The Mixtures B and B2 were found to be not far inferior to fresh cow's milk, but the Mixture D1 was even more promising. It contained only 10 per cent of dried skimmed milk, and the importance of its success was enhanced by the poor quality of the basic diets that it was supplementing. The drinks provided for the Ludwigshafen schoolchildren, who were from 7 to 11 years old, were the equivalent in calories of about 750 g. liquid, full-cream milk, and here again Mixture C2, which contained 10 per cent of skimmed milk, was obviously of high value. It was, however, to be preferred to the milkless Mixture C only because it had a better taste.

Recommendations for Future Work

It is obvious that the work described in this Report calls for repetition under more perfect conditions, with more complete facilities, and with different sources of protein. One of the most simple variations would be to substitute fat-extracted soya flour for the full-fat flour used. Even such a comparatively

simple change must, however, be made cautiously, because it now appears that the choice of method used for the fat extraction determines the subsequent degree of solubility of the soya protein (Mann and Briggs, 1950).

It will be essential also to specify, in terms as exact as knowledge at the time allows, details of all the raw materials and the processes to which they are subjected. From some recent work (p. 21) it seems that heating soya may improve its nutritive value without impairing the trypsin inhibitor, and the separate effects need further investigation.

Sufficient is already known about vitamin B_{12} (p. 23) to show that it must certainly be given serious consideration in the preparation of any complete diet from plant sources; its value when added to cereal and soya mixtures such as those which were used in Trial I has been shown for rats (Appendix E) and must be proved or disproved for children.

Two features were common to all the mixtures used in the trials described in this Report; the cereals were malted, and soya flour was used to provide a large part of the protein. It must be realized that the malting was an expedient whose value may be limited to the feeding of children unable to tolerate large amounts of starch. The evidence that newborn children must have a starch-free diet is not entirely satisfactory and needs re-examination; it is common and universal practice to include considerable amounts of starch in the diets of children a month or two old, and no harm is done. It may be found that, except possibly for the smallest children, the ordinary malting process is unnecessary; a modified process might be found adequate (p. 37) or the malting might be replaced by some method of simple cooking. One of the disadvantages that such changes might entail would be a deterioration in the keeping qualities of the mixtures. It was undoubtedly the high concentration of sugars which prevented bacterial action during storage in the mixtures that were used. A malt extract is probably too expensive for general use and this fact alone is a strong argument against its retention in the future, unless malted materials really have, as Liebig believed, some particular virtue. If malting is carried out, it should be done in such a way that the ratio of glucose to maltose is as high as possible. Care should be taken also to use strains of cereals which will give a high protein content to the finished malt; the variations in protein content which arise from using different varieties of barley, for instance, are considerable (Wokes, 1946). On the other hand, there seems no obvious reason why the process should not be extended to cereals such as maize or millet which are not usually malted.

It was perhaps inevitable that considerable stress should be laid in this Report on the importance of soya. The soya bean stands pre-eminent among plants for its high-fat, low-carbohydrate and very high-protein content. In the amino-acids of its protein the proportion of lysine is very high, making it especially suitable as a complementary food to cereals. For mixture with other staple foods it is perhaps not so exceptionally valuable, but throughout Europe the staple food is cereals.

Soya has been the subject of an immense amount of scientific and semi-scientific work; its literature is vast and includes a monthly journal. It has been used for the feeding of all kinds of livestock and of armies, and it has been brought to an important place in human nutrition, not merely in China and other Eastern countries where it has for many centuries been a staple food, but also in those European and American lands where the climate is suitable for its growth. There are almost certainly many other parts of the world in

which some of the thousand-odd varieties of the bean could be grown profitably. It is not the least of its virtues as a food for children that, in comparison with any source of animal protein except perhaps fish, it is cheap. Some poor results in the feeding of children and farm animals, and a peculiar unpleasantness in the taste, have caused reluctance to extend its use. The poor results may have been due in some instances to the presence of the trypsin inhibitor, but the trypsin inhibitor can be removed, as it was in the present series of trials, by prolonged steaming, and the steaming removes also the greater part of the objectionable taste. It is possible that methods of removing the inhibitor even simpler than steaming may be found since heating is not, apparently, essential (De and Ganguly, 1947). At the time of writing, although the inhibitor has been known for about five years, the commercial processing of soya flour for ordinary use is still limited to a short period of steaming which is not sufficient to destroy the inhibitor. It is to be hoped that the practice will be changed when more experimental work has demonstrated the necessity. It is true that many processes, such as the cooking of bread in which soya has been included, are probably drastic enough to bring about the destruction of the inhibitor, or at least to reduce its potency, but other processes, especially those employing dry heat or low temperatures, may not be adequate. It would be interesting to know if some of the much-advertised patent drinks at present marketed, which are known to contain soya, contain also the inhibitor. If they do, their protein value may be much less than that shown by ordinary analysis.

The actual and potential values of soya protein are undoubted, but they should not prevent an active search for other protein sources, which are likely to prove of value for supplementing readily available, protein-containing foods. One material of plant origin which promises well is sunflower-seed meal (see p. 32). It has already been shown to have considerable value as a food for children and the objection to its use, that the growth it produces falls off in rate after a short time, should be a stimulus to further investigation rather than a reason for abandoning it. The decline in growth rate may be a sign that the protein is incomplete but, if that is so, suitable supplementary protein from sources other than milk could be found. The possibility that the decline coincides with the exhaustion of a supply of the animal-protein factor should be explored too. The sunflower is one of the comparatively few plants yielding a high percentage of good protein which might, if necessity arose, be successfully cultivated in Britain (Blackman, 1948). Groundnut meal, although its amino-acid composition makes it theoretically slightly inferior to sunflower-seed meal (see Table 12, p. 46), is another protein-rich food which deserves a trial in infant feeding, and there must be many other foods which could be pressed into service for the completion of protein mixtures. The discovery that the Brazil nut is an extremely rich source of methionine (Horn, Jones and Blum, 1950), although it may have only a limited application, is a good instance of the way in which help may come from unexpected directions.

The supplementary proteins need not be of plant origin. At the present time, huge quantities of skimmed milk are being used, especially in the United States, in animal feeding or in various industrial processes unconnected with nutrition, or are being wasted altogether (Butler, 1942). Only a small proportion of the surplus is absorbed by such measures as the incorporation of milk solids into bread (Volz, Forbes, Nelson and Loosli, 1945). It seems very unfortunate that economic considerations such as the cost of drying and transport prevent much more of the skimmed milk protein from being used in

child feeding. There is little doubt that the experiments which established the value of adding cow's milk to a poor diet owed their success partly to the effect of protein supplementation, although protein supplementation was only one of the benefits conferred.

Another protein-containing material which must be tried as a food for children, and especially as a supplement for the cereals in their diets, is fish. Its supplementary value has been proved in animal feeding. Its proteins closely resemble those of meat and milk in composition (Beach, Munks and Robinson, 1943) and theoretically, therefore, it should be able to deputize for milk. Fish is also a good source of vitamin B_{12}, and its adaptation to child feeding offers another field for investigation which seems likely to yield valuable results. It should not be difficult to find some preparation of fish suitable for children.

As a source of protein, fish has in many parts of the world the great advantage over milk of being extremely cheap. There have been few references to price in this Report, but it has always been realized that unless the complete mixtures of plant proteins could be produced at prices not far above those of the locally available, incomplete plant products, the mixtures could have little hope of wide employment. Processing of any kind would have to be reduced to a minimum, or the processes used would have to be very cheap ones.

In many places, South Africa, the West Indies and Mexico, for example, condensed milk, often much diluted with water, is used by even the poorest native mothers for feeding their children. The fact, although it may portend the spread of food habits from the more highly developed communities, serves also to show how even in circumstances of poverty, money can be found for feeding the child. The same amount of money could undoubtedly be spent to greater advantage if the lessons of this Report were given practical application.

An objection to the use of plant protein mixtures frequently advanced is that they would not easily be accepted because of the conservative attitude of mothers and the well-known difficulties in the way of introducing dietary changes of any kind. The ubiquity of condensed milk is itself an answer to the objection, and it seems to be the opinion of many of those qualified to judge, that the problems of education into new ways, and into the use of new foods, could be overcome without much difficulty if the advantages of change were practically demonstrated to the mothers. Education would certainly be necessary, but the reorganization of feeding on the lines which this Report may have suggested goes far beyond education, and is an immense work which can only be accomplished if the powers of education, agriculture and industry, and their political machinery, can be made to work together for this one purpose.

APPENDIX A

Specimen of weekly diet sheet used at the Augustinusstift

Trial II	Bread	Butter	Vegetables		Thick *Brei*		Medium *Brei*	Thin *Brei*	Gisela . . . diet B2
					11 a.m.	4 p.m.			
Amounts offered (g.)	40 {	5·0* 3·5	}200		200	300	300	200	
Amounts consumed (g.)‡ September:			Calories†						
3	‡	7·50	130	74	130	‡ 150	‡ 0	‡	Appetite not good. Slight fever last night. Left ear tender.
4		6·75	100	57	100				
									Better.
5		6·85	105	58	105				
6		7·75	157	112	158	175			
7				114	200	0			
8				108	200				
9		6·55	85	48	85				
									Total	Percentage
Daily average (g.) ..	40	7·45			140	261	257	200		
Average Calories ..	100	60		82	176	327	242	125	1,112	100
Calories from:										
Protein	12					95	47	23	177	16
Fat	4	60		82		49	24	12	231	21
Carbohydrate	84					359	171	90	704	63
Cereal and soya mixture						241	116	60	417	37
Skimmed milk ..						68	33	17	118	11

*The upper and lower figures are the amounts of butter offered with bread and vegetables, respectively.
†With vegetables a column was necessary for calories because the calorie value of the vegetables differed from day to day.
‡If the total amount offered was eaten, no entry was made.

APPENDIX B

Record card used in the Trial with schoolchildren at Ludwigshafen

SEX								SCHOOL
NAME								CLASS
ADDRESS								DATE OF BIRTH

Date of examination	Height			Weight			Remarks
	Actual	Standard	Percent-age of standard	Actual	Standard	Percent-age of standard	

Date	Com-plexion	Posture	Develop-ment	Fat	Skin	Thyroid	GROUP	
							Remarks	Clinical grading

Attendances													
Week 1	2	3	4	5	6	7	8	9	10	11	12	13	Total

APPENDIX C

Ludwigshafen am Rhein, den 20. September 1948.

Die Ernährungsabteilung der Universität Cambridge, England, hat uns Lebensmittel angeboten, mit denen wir von jetzt ab bis Ende des Jahres 500 Kinder zusätzlich ernähren können. Wir haben aus der Goetheschule und Gräfenauschule die 500 Kinder ausgewählt, die sich im schlechtesten Ernährungszustand befinden und Ihr Kind gehört dazu. Da wir gerne feststellen wollen, welche Art Nahrung die beste für zukünftige Kinderspeisungen ist, geben wir jetzt vier Arten. Jedes Kind wird während der ganzen Zeit dieselbe Speise bekommen und es ist sehr wichtig, dass es regelmässig an der Speisung teilnimmt. Mit Hilfe der Schulverwaltung werden wir die Speise an sechs Tagen in der Woche ausgeben können (von Montag bis Samstag einschliesslich) und wir hoffen, dass auch Sie Ihr Möglichstes tun werden, dass Ihr Kind regelmässig kommt.

Würden Sie bitte Ihrem Kind ein Gefäss mitgeben, das ungefähr 1/2 Ltr. fasst, ausserdem einen Löffel. In jeder Portion sind 500 Kalorien enthalten und so können Sie sicher sein, dass es Ihrem Kind sehr zugute kommt, in welche Gruppe es auch kommt.

Mit freundlichen Grüssen!

Die Quäkerhilfe.

APPENDIX D

EXPERIMENTS WITH THE TRYPSIN INHIBITOR

An account of the discovery of the trypsin inhibitor in soya bean and a summary of the work which has established its chemical nature and its importance in nutrition, is given elsewhere (p. 19).

In the present work the effect of the inhibitor was measured *in vitro* by estimating the amount of amino-nitrogen set free by enzymic digestion from suspensions of various cereal and soya mixtures.

Three experiments are described. The first two compared Mixture B which contained the inhibitor with Mixture C in which the inhibitor had been destroyed. The third compared Mixture C1, a combination of Mixture C and milk, with Mixture C2, in which milk was incorporated during manufacture (see p. 59).

The mixtures were shaken with water for one hour at room temperature and brought to *p*H 8·3 with NaOH, and a veronal buffer was added to maintain this *p*H. They were then warmed rapidly to 37° C. and incubated with a solution of trypsin at that temperature. Samples were removed for titration with formol at intervals of twenty minutes. The amounts of material taken for each experiment contained 750 mg. of nitrogen.

Experiment 1

Fig. 8(*a*) shows the different amounts of amino-nitrogen released from the cereal and soya Mixtures B and C and from a combination of 90 per cent of Mixture B with 10 per cent of dried skimmed milk. Skimmed milk by itself was included for comparison. The inhibitor is envisaged as a protein which combines with a set weight of enzyme, irrespective probably of the total amount of protein present. The removal of the inhibitor caused an improvement about equal to that produced by introducing the 10 per cent of milk. The result of this experiment should be compared with that of the rat experiments shown in Fig. 9(*c*).

Experiment 2

In Trial II (pp. 76, 87) 25 per cent of dried skimmed milk powder was added to 75 per cent of Mixture B for one of the diets. In Experiment 2 this combination and two other combinations with different proportions of milk were compared with similar combinations of Mixture C with milk (Fig. 8(*b*)). In each of the three tests the release of amino-nitrogen was greater with Mixture C from which the inhibitor was absent. The amounts released from Mixture B with milk were only about 60 per cent of the theoretical maximum calculated from a further experiment in which this mixture and the skimmed milk were digested separately. The amounts released from Mixture C with milk were, however, very near to the theoretical maximum.

Experiment 3

Mixture C1, the combination of 90 parts Mixture C with 10 parts dried skimmed milk which was used at Ludwigshafen, was compared with Mixture C2 which was used at Ludswigshafen and also in Trial II at the Augustinusstift. In both the trypsin inhibitor had been destroyed, and in both the amount of amino-nitrogen released was about the same.

At Ludwigshafen, where the children were from 7 to 11 years old, Mixture C2 gave results which were comparable with those given by Mixture C1, but at the Augustinusstift, where the children were younger, Mixture C2 was inferior to the plain Mixture C in which the inhibitor had been destroyed but which contained no milk. The Ludwigshafen results agree with the findings *in vitro*, and the agreement suggests that the protein values of Mixtures C1 and C2 might have been equal if the protein was fully absorbed. Mixture C2, however, caused the children to have loose stools and its protein was probably absorbed poorly in consequence. Almost certainly, it was the carbohydrate, and not the protein, of Mixture C2 which was at fault (see p. 125).
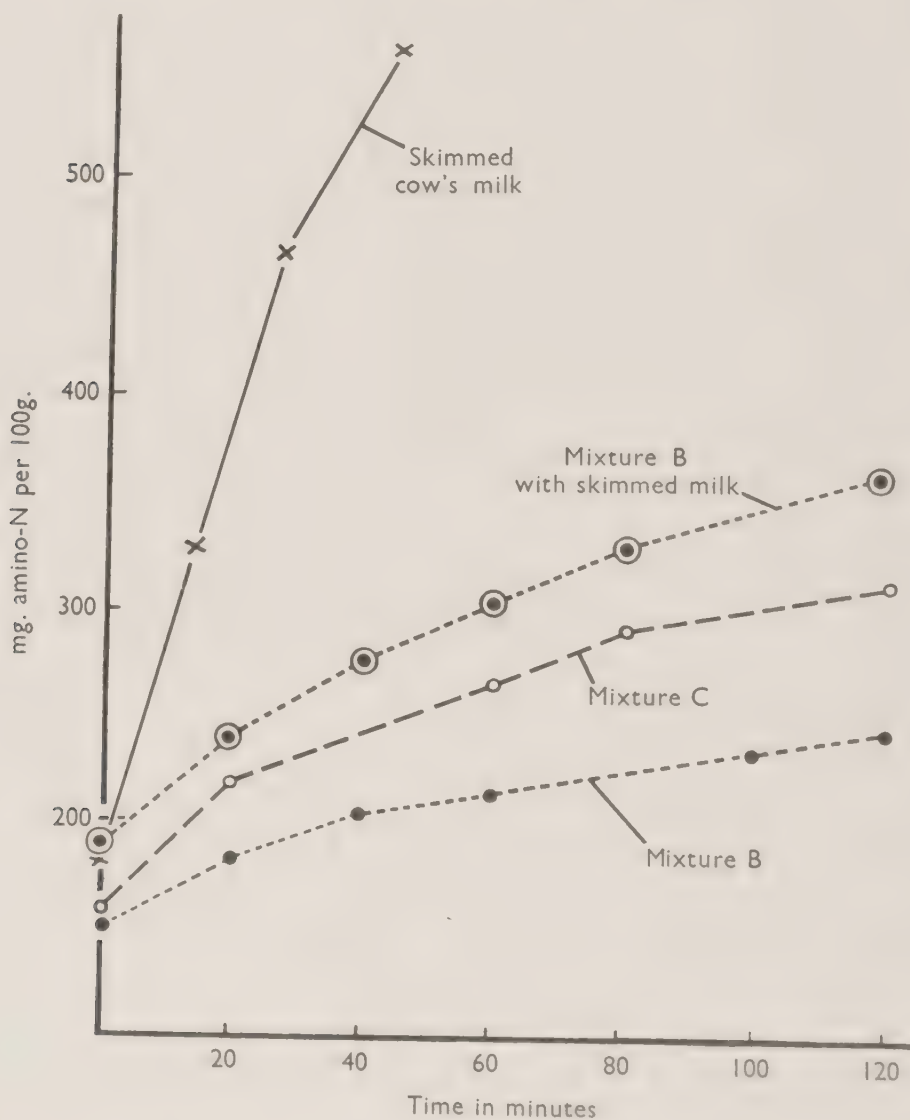
FIG. 8(a).

Rate of liberation of amino-nitrogen on incubating various cereal and soya mixtures, and skimmed milk, with trypsin. Mixture B contained the trypsin inhibitor, but it had been destroyed in Mixture C. Larger amounts of amino-acids were released from Mixture C. The addition of 10 per cent of skimmed milk to Mixture B caused an increase about equal to that caused by destruction of the inhibitor.
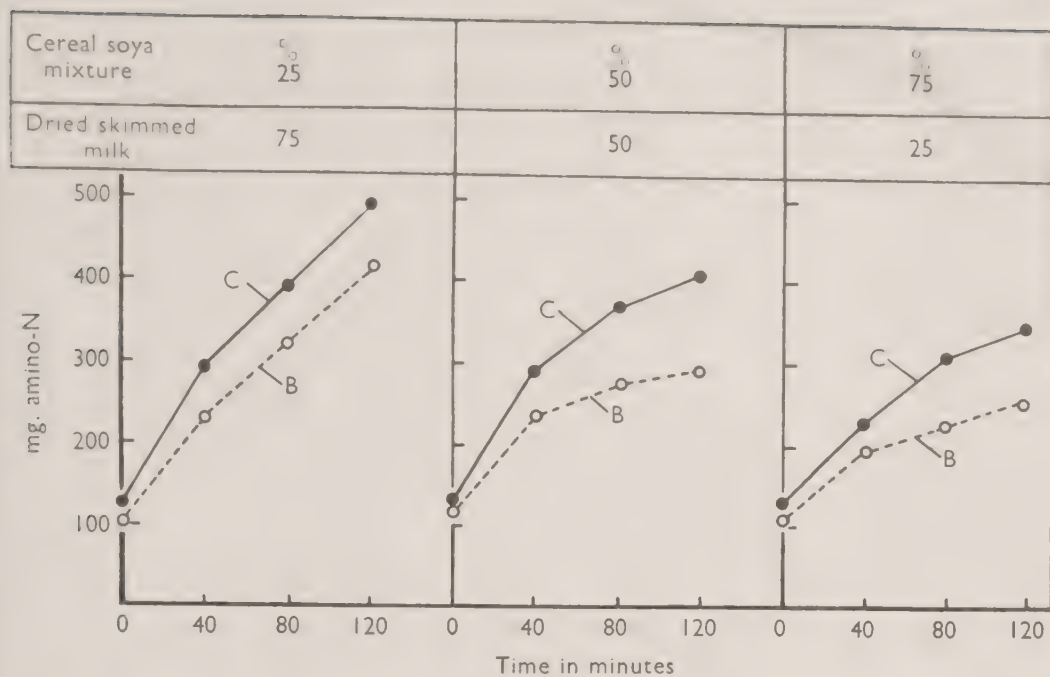
FIG. 8(b).

Rate of liberation of amino-nitrogen on incubating different combinations of cereal and soya Mixtures B and C and dried skimmed milk, with trypsin. The amount of amino-acids released from the combinations containing Mixture B was always less than that released from the combinations containing Mixture C, in which the trypsin inhibitor had been destroyed.

APPENDIX E

GROWTH EXPERIMENTS ON RATS WITH THE CEREAL
AND SOYA MIXTURES

The cereal and soya mixtures were tested on young rats in experiments of two types.

In Experiments 1, 2, 3 and 4 the cereal and soya mixtures were used exactly as for the groups of children from 1 to 2 years old; the mixtures were incorporated into the diet as *Brei* and, wherever possible, the rats were fed on samples representative of the children's whole diets. Mixtures A, B and C were all tested in this way, with and without addition of different amounts of skimmed milk. (For composition of the mixtures and other details, see p. 58.) A positive control diet was used as for the children, containing whole milk instead of the cereal and soya mixtures.

In Experiments 5 and 6 the cereal and soya mixtures were given as the only source of protein in the same way as was done by Chick and Slack (1946) when testing malted foods for babies on rats (p. 50). The composition of the diets and of the positive control diets used is shown in Table 45.

The rats in all the experiments received food to appetite, and in addition two drops daily of the preparation of vitamins A and D which was given to the children (p. 53).
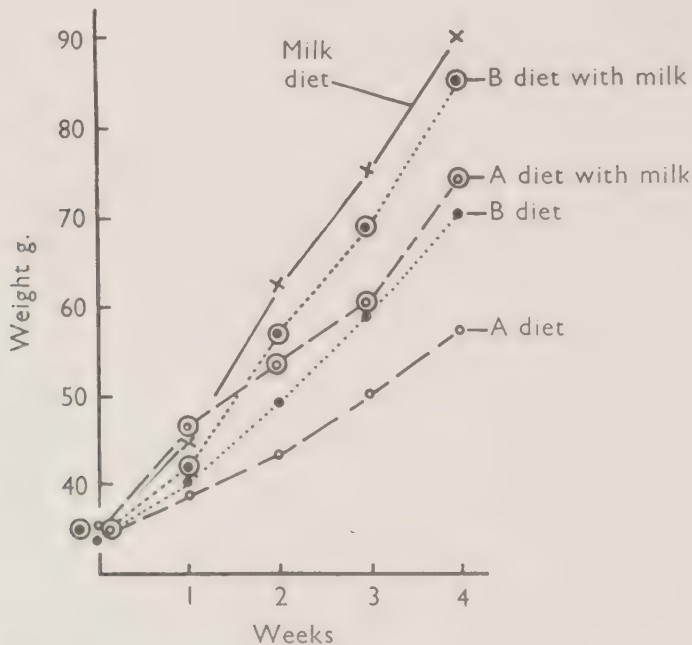
FIG. 9(*a*). *Experiment* 1.

Rate of weight increase of rats given the diets which were used for the children of from 1 to 2 years old in Trial I and similar diets including some skimmed milk. These diets contained different percentages of protein:

Control milk diet	11
Mixture B diet	13
Mixture A diet	9
Mixture B diet with skimmed milk	15
Mixture A diet with skimmed milk	11

For the diets containing skimmed milk, 10 parts of the milk powder were added to every 90 parts of the cereal and soya mixture. The additions were clearly beneficial.

TABLE 45

Composition of the diets used in Experiments 5 and 6 (Figs. 9 (e) and 9 (f))

Diet	Total protein (per cent)	Amounts of constituents						
		Cereal and soya Mixture A (g.)	Cereal and soya Mixture B (g.)	Dried skimmed milk (g.)	Yeast (g.)	Dextrin (g.)	Lard (g.)	Salt mixture† (g.)
Experiment 5								
Mixture A*	10·0	100	—	—	—	—	2	1
Mixture B	10·0	—	54	—	—	46	2	1
Milk control	10·0	—	—	29	1	70	2	1
Experiment 6								
Mixture B	17·5	—	100	—	—	—	2	1
Mixture B with milk ..	19·0	—	90	10	—	—	2	1

* For composition of the cereal and soya mixtures see p. 58.
† British Drug Houses, Ltd.

FIG. 9(b). *Experiment* 2.

Rate of weight increase of rats given experimental cereal and soya mixtures of type B containing soya which had been treated by autoclaving (A) or steaming (S) to remove the trypsin inhibitor. Both variants gave identical results, which were better than those given by the ordinary Mixture B (black dots). This contained the inhibitor. The addition of 10 per cent dried milk to the mixture made with steamed soya caused further improvement.
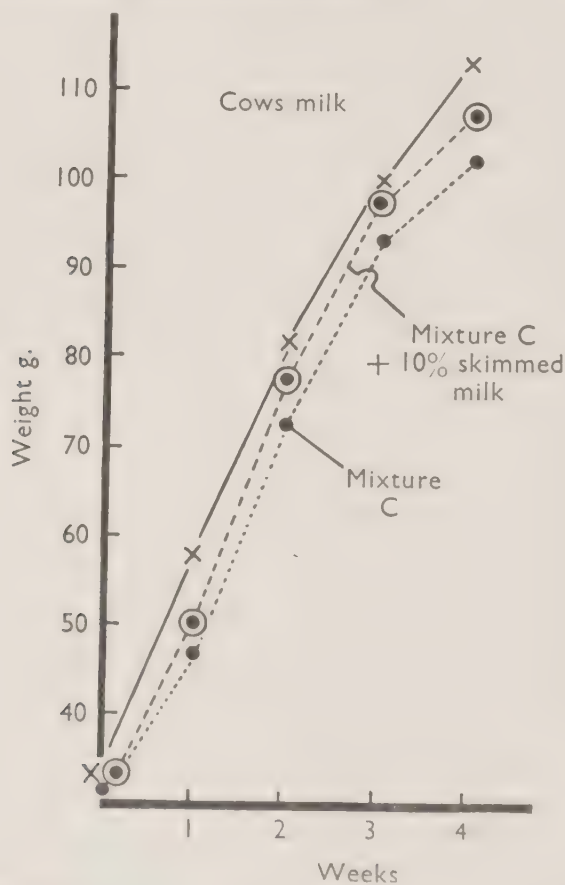
FIG. 9(c). *Experiment* 3.

Rate of weight increase of rats given diets made with Mixture C produced on the laboratory scale, under carefully controlled conditions, the trypsin inhibitor being removed by steaming. Growth was good, and even better when 10 per cent dried skimmed milk was added to the mixture.

Weanling rats were used weighing from 25 to 40 g. They were usually kept singly, but in some experiments two or three of the same sex were kept in one cage. The total number of rats in any group was between six and ten. The rats were weighed twice a week. Experiments 1 to 5 lasted 4 weeks, Experiment 6 lasted 26 weeks. After 17 weeks, 3 μg. vitamin B_{12} (Glaxo) were given by intramuscular injection daily for 3 days to one of the groups of rats.

The results are summarized in Table 46 and are shown graphically in Figs. 9(a) to 9(f).

Conclusions

The addition of dried skimmed milk to the Mixtures A and B (Experiments 1 and 2) was clearly valuable. The addition of vitamin B_{12} to Mixture B produced a marked increase in growth rate (Experiment 6).

Mixture B was always superior to Mixture A, even when the amounts of protein in the diet were equalized (Experiments 1 and 5).

The removal of the trypsin inhibitor from the soya in Mixture C increased the value of the mixtures (Experiment 3), but the good effects were nullified when the mixture was damaged by faulty manufacture (Experiment 4).
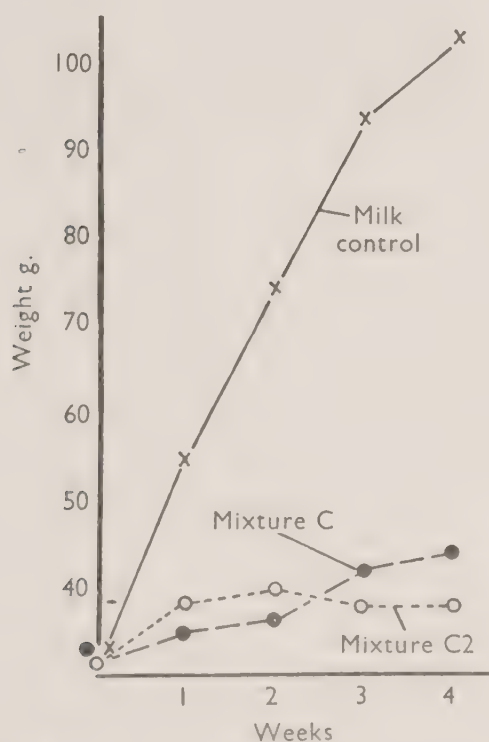
FIG. 9(d). *Experiment* 4.

Rate of weight increase of rats given diets made with Mixtures C and C2 produced on the full commercial scale. The mixtures were probably spoilt by overheating. Milk was incorporated into Mixture C2 during manufacture, but its value was obviously lost.

TABLE 46

Summary of rat growth experiments with the cereal and soya mixtures used for the children

Experiments in which the diets were samples of those given to the children with the cereal and soya mixtures incorporated as *Brei*.

Experiment No.	Object	Result	Comment
1.	To compare the diets of the children given cereal and soya Mixtures A and B in Trial I, and to find the value of adding small amounts of dried skimmed milk to the mixtures.	The Mixture A diet gave a very poor result (*Fig.* 9(*a*)). The Mixture B diet was better, and the milk diet best. When 10 per cent of the cereal and soya mixture was replaced by 10 per cent dried skimmed milk, growth was considerably accelerated, but the control milk diet was still the best.	The diets used were samples of those actually eaten by the children. The percentage of calories from total protein in the diets was 9 for the Mixture A diet, 13 for the Mixture B diet, and 11 for the milk diet (Table 32). The combination of 90 parts of Mixture A or of Mixture B with 10 parts of dried skimmed milk, increased the amount of calories from total protein in the diets by about 2 per cent.
2.	To compare diets made with Mixture B (as used in Experiment 1) with diets exactly similar, except that the soya used for the Mixture was treated by autoclaving at 120 C. for 15 min. or by steaming for 100 min. These procedures removed the trypsin inhibitor (p.19).	Removing the inhibitor greatly increased the value of Mixture B for rat growth (*Fig.* 9(*b*)). The two methods of removal gave identical results. Replacing 10 per cent of the cereal and soya mixture containing steamed soya by 10 per cent dried skimmed milk brought about further improvement.	The method of removing the inhibitor by steaming was finally adopted as it was simpler and did not require special apparatus.
3.	To find the value of a diet containing Mixture C made as described (p. 59), but under laboratory conditions with close control of temperature.	Value for rat growth was very high (*Fig.* 9(*c*)). Incorporating fresh skimmed milk into the mixture before drying caused a further small improvement.	Because of the success of this experiment, it was decided to use Mixture C, and without skimmed milk incorporated (Mixture C2) in Trial III.
4.	To find the value of Mixtures C and C2 made on a large scale.	Value for rat growth very low, probably because there had been overheating (*Fig.* 9(*d*)).	Even the incorporation of milk failed to produce a successful food. These batches of Mixtures C and C2 were discarded, and new batches, made more carefully, were used in Trial III.

Experiments in which the cereal and soya mixtures were the only source of protein.

Experiment No.	Object	Result	Comment
5.	To repeat the original experiment of Chick and Slack (1946) (p. 50), with the cereal and soya Mixtures A and B.	Both mixtures gave poor results, compared with milk, but Mixture B was slightly superior to Mixture A (*Fig.* 9(*e*)).	The composition of the diets is given in Table 45. Mixture A should have been similar to the diet No. 7A used by Chick and Slack, but gave widely different results. The reason for the difference is unknown. The rats receiving Mixture A did not have diarrhoea, although this was one of the chief causes of failure with the mixture when it was eaten by the children in Trial I (p. 83).
6.	To find the value of adding vitamin B_{12} to Mixture B.	The growth rate was improved (*Fig.* 9(*f*)).	The experiment was originally designed to investigate the value for prolonged growth of Mixture B, and of a combination of 90 per cent Mixture B with 10 per cent dried skimmed milk.
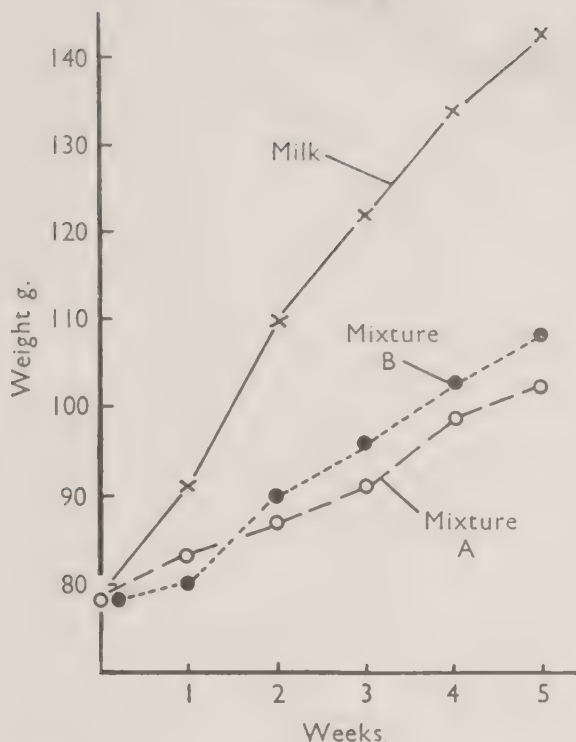
FIG. 9(*e*). *Experiment 5.*
Rate of weight increase of rats given the cereal and soya Mixtures A and B and a skimmed milk diet. Each of the diets contained 10 per cent protein (Table 45). There was a wide discrepancy between the growth of the rats given milk and that of the rats given the mixtures.
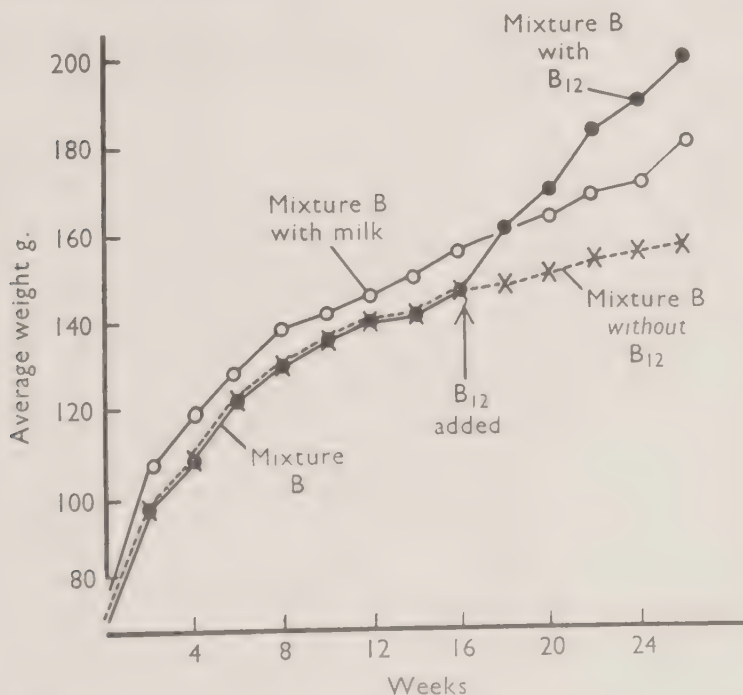
FIG. 9(*f*). *Experiment 6.*
Rate of weight increase of rats given Mixture B or a combination of 90 parts Mixture B with 10 parts dried skimmed milk (Table 45). In the seventeenth week the Mixture B group was divided into two sub-groups. One sub-group was given 3 μg. vitamin B_{12} by intramuscular injection daily for 3 days. The growth rate increased. The group given the combination of Mixture B and milk grew a little better than the group given Mixture B only but were surpassed by the sub-group given vitamin B_{12}.

SUMMARY

1. The literature was searched for evidence about the possibility of preparing from plant materials a suitable substitute for human or cow's milk in infant feeding. Nothing in the composition of either milk revealed any reason why plant sources should not be able to provide a satisfactory alternative.

2. Protein presents the most complicated part of the problem. Variations in the composition of the plant, and in the methods of preparing and storing the products, bring about changes in the amount of the protein and in the availability of its amino-acids. Nevertheless, animal experiments have shown that combinations of naturally occurring plant proteins can be arranged to yield mixtures of amino-acids of high biological value. Other experiments have shown the possibility of applying such knowledge to human nutrition.

3. Some experiments of Chick and Slack (1946) showed that the proteins of a mixture of barley, wheat and soya, with the cereals malted, had a biological value for rats near to that of the proteins in cow's milk. An investigation was made into the effects of feeding children on similar mixtures.

4. The investigation was carried out in Germany between late 1947 and early 1949, at a Roman Catholic orphanage in Wuppertal, at the Town Orphanage in Duisburg, at two schools in Ludwigshafen-am-Rhein, and at the Landesfrauenklinik der Rheinprovinz, Wuppertal.

5. About 25 newborn children, 25 aged from 6 to 12 months, 50 aged from 1 to 2 years, 50 aged from 2 to 6 years, and 625 aged from 7 to 11 years, took part at various times. The plan which was usually followed was to divide the children into groups, all of which received the same basic diet, and to add one of the mixtures or cow's milk. The home diets of the schoolchildren, who were given a mid-day meal, could not be controlled, but the full diets of the other children were known and recorded.

6. Three combinations of barley, wheat and soya, four of barley, wheat and soya with different amounts of milk incorporated, and two of barley, maize and soya with milk, were tested for periods of between 8 and 24 weeks. The soya in most of the mixtures was treated to remove the trypsin inhibitor. Two of the combinations were discarded because they caused gastro-intestinal upsets.

7. Variations in the manufacture of the mixtures, and illness unconnected with the diet, caused difficulty in interpreting the results. It was shown, however, that, for children of up to 1 year old, about half the milk in the diet could be replaced by the mixtures.

8. For children of from 1 to 2 years old, at least two of the mixtures seemed to be nearly perfect substitutes for all the milk in the diet.

9. For children of from 2 to 6 years old, nearly all the mixtures gave good results, despite the poor quality of the basic diet they were supplementing, but for optimum growth a small amount of milk in addition seemed to be necessary.

10. A similar result was obtained with the children aged from 7 to 11 years. A cereal and soya mixture with a small amount of milk incorporated gave results as good as those of an equicaloric supplement of full-cream milk.

11. The calorie intake of children of from 40 to 125 weeks old was studied in detail, and a relation was shown between the intake and the weight for age. The intake was greater the more underweight the child was.

12. The varying effectiveness of the cereal and soya mixtures did not seem to depend on differences in their amino-acid composition so much as on variations in the method of manufacture. The variations may have affected the carbohydrate more than the protein.

13. It was considered that the results of the investigation showed that adequate substitutes for milk could probably be provided from plant sources, and that the boundary zone between success and failure, however narrow it might be in experiments with a fast-growing animal such as the rat, was much wider in the feeding of the human child.

14. Other combinations of plant foods and other methods of making them suitable for child feeding should be tried. The effect of adding vitamin B_{12} is another and highly important subject for research.

ACKNOWLEDGEMENTS

BIBLIOGRAPHY

ABRAHAM, G. (1928). Milchlose Ernährung im Säuglingsalter. *Arch. Kinderheilk.*, **84**, 36.

ALBANESE, A. A. (1947). The amino acid requirements of man. *Advanc. Protein Chem.*, 3, 272.

ALBANESE, A. A., HIGGONS, R. A., VESTAL, B. and STEPHANSON, L. (1950). Phenylalanine requirements of children. *Fed. Proc.*, 9, 144.

ALBANESE, A. A., HOLT, L. E. Jr., BRUMBACK, J. E. Jr., FRANKSTON, J. E. and IRBY, V. (1944). Observations on a diet deficient in both methionine and cystine in man. *Johns Hopk. Hosp. Bull.*, **74**, 308.

ALBANESE, A. A., HOLT, L. E. Jr., DAVIS, V. I., SNYDERMAN, S. E., LEIN, M. and SMETAK, E. M. (1948). The isoleucine requirement of the infant. *J. Nutr.*, **35**, 177.

ALBANESE, A. A., HOLT, L. E. Jr., DAVIS, V. I., SNYDERMAN, S. E., LEIN, M. and SMETAK, E. M. (1949). The sulfur amino requirement of the infant. *J. Nutr.*, **37**, 511.

ALBANESE, A. A., HOLT, L. E. Jr., IRBY, V., SNYDERMAN, S. E. and LEIN, M. (1947a). Studies on the protein metabolism of the infant. 1. The comparative biological value of some milk protein preparations. *Johns Hopk. Hosp. Bull.*, **80**, 149.

ALBANESE, A. A., HOLT, L. E. Jr., IRBY, V., SNYDERMAN, S. E. and LEIN, M. (1947b). Studies on the protein metabolism of infants. 2. Tryptophane requirement of the infant. *Johns Hopk. Hosp. Bull.*, **80**, 158.

ALBANESE, A. A., SNYDERMAN, S. E., LEIN, M., SMETAK, E. M. and VESTAL, B. (1949). The biological value of corn and wheat proteins in the male infant, with a note on the utilization of D-tryptophan. *J. Nutr.*, **38**, 215.

ALLISON, J. B. (1949). Biological evaluation of proteins. *Advanc. Protein Chem.*, **5**, 155.

ANDERSEN, D. H. (1942). Pancreatic enzymes in the duodenal juice in the celiac syndrome. *Amer. J. Dis. Child.*, **63**, 543.

ANDRÉ, E. (1928). L'aleurone des graines oléagineuses substance alimentaire. *C. R. Acad. Agric. Fr.*, **14**, 1292.

BAERNSTEIN, H. D. (1937–8). The nutritional value of various protein fractions of the peanut. *J. biol. Chem.*, **122**, 781.

BAHRDT, H. (1914). Ernährungsversuche mit Friedenthalscher Milch. *Z. Kinderheilk.*, *Orig.*, **10**, 303.

BARENBERG, L. H. and ABRAMSON, H. (1930). The effect of large amounts of milk sugar on the stools and nutrition of infants. *Arch. Pediat.*, **47**, 1.

BARKI, V. H., DERSE, P. H., COLLINS, R. A., HART, E. B. and ELVEHJEM, C. A. (1949). The influence of coprophagy on the biotin and folic acid requirements of the rat. *J. Nutr.*, **37**, 443.

BARNES, R. H., BATES, M. J. and MAACK, J. F. (1946). The growth and maintenance utilization of dietary protein. *J. Nutr.*, **32**, 535.

BAUMGARTEN, W., MATHER, A. N. and STONE, L. (1946). Essential amino acid composition of feed materials. *Cereal Chem.*, **23**, 135.

BEACH, E. F. (1948). Proteins in nutrition (historical). Chapter 1 in *Proteins and amino acids in nutrition*, ed. by M. Sahyun. Reinhold Publishing Corporation, New York.

BEACH, E. F., BERNSTEIN, S. S. and MACY, I. G. (1941). Intake of amino acids by breast-milk-fed infants and amino acid composition of cow's milk and human milk. *J. Pediat.*, **19**, 190.

BEACH, E. F., MUNKS, B. and ROBINSON, A. (1943). The amino acid composition of animal tissue protein. *J. biol. Chem.*, **148**, 431.

BEACH, E. F. and WHITE, A. (1937). Methionine as the limiting factor of arachin. *J. biol. Chem.*, **119**, viii.

BEADLES, J. R., BRAMAN, W. W. and MITCHELL, H. H. (1930). The cystine deficiency of the proteins of garden peas and of potatoes. *J. biol. Chem.*, **88**, 615.

BECKER, C. (1934). Soya bei eitrigen Harninfektionen, Ekzem und Diabetes. *Arch. Verdaukr.*, **56**, 260.

BEESON, W. M., LEHRER, W. P. Jr. and WOODS, E. (1947). Peas supplemented with wheat germ or corn germ, as a source of protein for growth. *J. Nutr.*, **34**, 587.

BELL, D. H. (1950). Personal communication. Dept. Biochemistry, Univ. Cambridge.

BERGEIM, O. (1926). Intestinal chemistry. 5. Carbohydrates and calcium and phosphorus absorption. *J. biol. Chem.*, **70**, 35.

BEST, C. H. and LUCAS, C. C. (1950). Choline malnutrition. In *Clinical nutrition*, ed. by N. Jolliffe, F. F. Tisdall and P. R. Cannon. Paul B. Hoeber, New York.

BIRD, H. R. and BURKHARDT, G. J. (1943). Factors affecting the nutritive value of soybean oil meals and soy beans for chickens. *Bull. Md agric. Exp. Sta.*, A27, p. 35.

BLACKFAN, K. D. and WOLBACH, S. B. (1933). Vitamin A deficiency in infants. A clinical and pathological study. *J. Pediat.*, **3**, 679.

BLACKMAN, G. E. (1948). The future of oil seed crops. *Farming, Lond.*, **2**, 205.

BLAZSÓ, S. (1938–9). Zum Schwefel- und Eiweissstoffwechsel des näturlich und künstlich ernährten Säuglings. *Ann. paediat.*, **152**, 302.

BLOCK, R. J. (1933). The basic amino acids of serum proteins. *J. biol. Chem.*, **103**, 261.

BLOCK, R. J. and BOLLING, D. (1945). *The amino acid composition of proteins and foods*. Charles C. Thomas, Springfield, Ill.

✓ BLOCK, R. J. and BOLLING, D. (1946). The amino acid composition of cow and human milk proteins. *Arch. Biochem.*, **10**, 359.

BLOCK, R. J., CANNON, P. R., WISSLER, R. W., STEFFEE, C. H. Jr., STRAUBE, R. L., FRAZIER, L. E. and WOOLRIDGE, R. L. (1946). The effects of baking and toasting on the nutritional value of proteins. *Arch. Biochem.*, **10**, 295.

BLOCK, R. J., JONES, D. B. and GERSDORFF, C. E. F. (1934). The effect of dry heat and dilute alkali on the lysine content of casein. *J. biol. Chem.*, **105**, 667.

✓ BLOCK, R. J. and MITCHELL, H. H. (1946–7). The correlation of the amino-acid composition of proteins with their nutritive value. *Nutr. Abstr. Rev.*, **16**, 249.

BOAS-FIXSEN, M. A. (1934–5). The biological value of protein in nutrition. *Nutr. Abstr. Rev.*, **4**, 447.

BOAS-FIXSEN, M. A. and JACKSON, H. M. (1932). The biological value of proteins. 4. The biological values of the proteins of wheat, maize and milk. *Biochem. J.*, **26**, 1923.

BORCHERS, R. and ACKERSON, C. W. (1947). Trypsin inhibitor. 4. Occurrence in seeds of the *Leguminosae* and other seeds. *Arch. Biochem.*, **13**, 291.

BORCHERS, R., ACKERSON, C. W. and MUSSEHL, F. E. (1948a). Trypsin inhibitor. 8. Growth inhibiting properties of a soybean trypsin inhibitor. *Arch. Biochem.*, **19**, 317.

BORCHERS, R., ACKERSON, C. W. and MUSSEHL, F. E. (1948b). Trypsin inhibitor. 6. Effect of various heating periods on the growth promoting value of soybean oil meal for chicks. *Poult. Sci.*, **27**, 601.

BORCHERS, R., ACKERSON, C. W. and SANDSTEDT, R. M. (1947). Trypsin inhibitor. 3. Determination and heat destruction of trypsin inhibitor of soybeans. *Arch. Biochem.*, **12**, 367.

BORCHERS, R., HAM, W. E., SANDSTEDT, R. M., ACKERSON, C. W., THAYER, R. H. and MUSSEHL, F. E. (1947). Trypsin inhibitor. 5. Nutritive value of treated soybean oil meal and some characteristics of the trypsin inhibitor in soybeans. *Res. Bull. Univ. Neb. agric. Exp. Sta.*, No. 152.

BOUTWELL, R. K., GEYER, R. P., ELVEHJEM, C. A. and HART, E. B. (1943). Further studies on the growth-promoting value of butter fat. *J. Dairy Sci.*, **26**, 429.

BOWMAN, D. E. (1943). The ether soluble fraction of navy beans and the digestion of starch. *Science*, **98**, 308.

BOWMAN, D. E. (1944). Fractions derived from soy beans and navy beans which retard digestion of casein. *Proc. Soc. exp. Biol., N.Y.*, **57**, 139.

BOWMAN, D. E. (1945). Further observations on the trypsin retarding fractions of navy and other beans. *Fed. Proc.*, **4**, 84.

BOWMAN, D. E. (1946). Differentiation of soybean antitryptic factors. *Proc. Soc. exp. Biol., N.Y.*, **63**, 547.

BOWMAN, D. E. (1948). Further differentiation of bean trypsin-inhibiting factors. *Arch. Biochem.*, **16**, 109.

BOYNTON, B. (1936). Measurements of weight and length of girls 2–48 months old. *Univ. Ia Stud. Child Welf.*, No. 325.

BRANSBY, E. R. (1950). Personal communication. Ministry of Health, Whitehall, London, S.W.1.

✓ BRANSBY, E. R., BRANSBY, N. B., KON, S. K., MAWSON, E. H. and ROWLAND, S. J. (1950). A study of the composition of milk throughout an individual lactation of 33 weeks. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 269, p. 141.

BRICKER, M., MITCHELL, H. H. and KINSMAN, G. M. (1945). The protein requirements of adult human subjects in terms of the protein contained in individual foods and food combinations. *J. Nutr.*, **30**, 269.

BRIGGS, A. P. (1922). A modification of the Bell-Doisy phosphate method. *J. biol. Chem.*, **53**, 13.

BRIGGS, D. R. and MANN, R. L. (1950). An electrophoretic analysis of soybean protein. *Cereal Chem.*, **27**, 243.

BROWN, W. L. (1942). The threonine, serine, cystine and methionine content of peanut proteins. *J. biol. Chem.*, **142**, 299.

BROWN, W. R., HANSEN, A. E., BURR, G. O. and McQUARRIE, I. (1938). Effects of prolonged use of extremely low-fat diet on an adult human subject. *J. Nutr.*, **16**, 511.

BROCK, J. F. and AUTRET, M. (1952). Kwashiorkor in Africa. FAO Nutritional Studies No. 8. *Bull. World Hlth Org.*, **5**, 1.

BURR, G. O. and BURR, M. M. (1929). A new deficiency disease produced by the rigid exclusion of fat from the diet. *J. biol. Chem.*, **82**, 345.

BURR, G. O. and BURR, M. M. (1930). On the nature and role of the fatty acids essential in nutrition. *J. biol. Chem.*, **86**, 587.

BUTLER, A. M. (1942). Nutritional requirements in infancy and in childhood. *Amer. J. Dis. Child.*, **64**, 898.

CADOGAN, W. (1753). An essay upon nursing, and the management of children from their birth to three years of age. J. Roberts, London.

✓ CAHILL, W. M., SCHROEDER, L. J. and SMITH, A. H. (1944). Digestibility and biological value of soybean protein in whole soybeans, soybean flour and soybean milk. *J. Nutr.*, **28**, 209.

CARLSON, C. W., MILLER, R. F., PEELER, H. T., NORRIS, L. C. and HEUSER, G. F. (1949). The complex nature of the animal protein factor. *Poult. Sci.*, **28**, 750.

CARLSON, S. C., HAFNER, F. H. and HAYWARD, J. W. (1946). Effect of soy flour and nonfat dry milk solids in white bread on the nutritional quality of the protein as measured by three biological methods. *Cereal Chem.*, **23**, 305.

CARY, C. A. and HARTMAN, A. M. (1947). Unidentified nutrients. *Yearb. U.S. Dep. Agric.* 1943–7, p. 779.

CHANG, I. C. L. and MURRAY, H. C. (1949). Biological value of the proteins and the mineral, vitamin and amino acid content of soymilk and curd. *Cereal Chem.*, **26**, 297.

CHANG, L. T., LI, H. C. and LAN, T. H. (1941). Biological values of soybeans protein and mixed soybean-pork and soybean-egg protein in human subjects. *Chin. J. Physiol.*, **16**, 83.

CHANG, K. and TSO, E. (1931). A soluble soybean milk powder and its adaptation to infant feeding. *Chin. J. Physiol.*, **5**, 199.

CHAPIN, H. D. and KAST, L. (1918). Preliminary report on the use of vegetable milk in children. *Trans. Amer. pediat. Soc.*, **30**, 160.

CHASE, B. W. and LEWIS, H. B., (1934). Comparative studies of the metabolism of amino acids. 6. The rate of absorption of leucine, valine and their isomers from the gastrointestinal tract of the white rat. *J. biol. Chem.*, **106**, 315.

CHERNICK, S. S., LEPKOWSKY, S. and CHAIKOFF, I. L. (1948). A dietary factor regulating the enzyme content of the pancreas: changes induced in size and proteolytic activity of the chick pancreas by the ingestion of raw soy-bean meal. *Amer. J. Physiol.*, **155**, 33.

CHICK, H., BOAS-FIXSEN, M. A., HUTCHINSON, J. C. D. and JACKSON, H. M. (1935). The biological value of proteins. 7. The influence of variation in the level of protein in the diet and of heating the protein on its biological value. *Biochem. J.*, **29**, 1712.

CHICK, H. and SLACK, E. B. (1946). Malted foods for babies. Trials with young rats. *Lancet*, **ii**, 601.

CHICK, H. and SLACK, E. B. (1948). Further observations on the nutritive value of the proteins contained in wheat flours of different extraction rates. *Brit. J. Nutr.*, **2**, 205.

CLEMENTS, F. W. (1949). *Infant nutrition.* John Wright and Sons, Ltd., Bristol.

COX, W. M. Jr. and MUELLER, A. J. (1937). The composition of milk from stock rats and an apparatus for milking small laboratory animals. *J. Nutr.*, **13**, 249.

CSÁKY, T. Z. (1947). Improving the biological value of bread made with corn (maize) flour, by the addition of extracted sunflower meal. *Arch. biol. hung.*, Ser. 2, **17**, 319.

CSONKA, F. A. (1937). Amino acids in staple foods. I. Wheat (*Triticum vulgare*). *J. biol. Chem.*, **118**, 147.

CSONKA, F. A. and JONES, D. B. (1933). Differences in the amino acid content of the chief protein (glycinin) from seeds of several varieties of soybean. *J. agric. Res.*, **46**, 51.

CSONKA, F. A. and JONES, D. B. (1934). The cystine, tryptophane, and tyrosine content of the soybean. *J. agric. Res.*, **49**, 279.

CUNHA, T. J., HOPPER, H. H., BURNSIDE, J. E., PEARSON, A. M., GLASSCOCK, R. S. and SHEALY, A. L. (1949). Effect of vitamin B_{12} and APF supplement on methionine needs of the pig. *Arch. Biochem.*, **23**, 510.

CUNHA, T. J., BURNSIDE, J. E., BUSCHMAN, D. M., GLASSCOCK, R. S., PEARSON, A. M. and SHEALY, A. L. (1949). Effect of vitamin B_{12}, animal protein factor and soil for pig growth. *Arch. Biochem.*, **23**, 324.

CZERNY, A. and KELLER, A. (1925). *Des Kindes Ernährung, Ernährungsstörungen und Ernährungstherapie.* F. Deuticke, Leipzig and Vienna.

DAVIES, J. N. P. (1952). Nutrition and nutritional diseases. *Annu. Rev. Med.*, **3**, 99.

DAVIES, W. L. (1939). *The chemistry of milk.* 2nd ed. Chapman and Hall, London.

DAY, P. L. (1935). Blood sugar in rats in which cataract was produced by a vitamin C-deficient diet and by a lactose-containing diet. *J. biol. Chem.*, **109**, xxvi.

DAY, P. L. (1936). Blood sugar in rats rendered cataractous by dietary procedures. *J. Nutr.*, **12**, 395.

DAY, H. G. and LEVIN, E. (1945). The nutritional value of sunflower seed meal. *Science*, **101**, 438.

DE, S. S., DESIKACHAR, H. S. R., DUDANI, A. T., KARNANI, B. T. and SUBRAHMANYAN, V. (1947). Rice gruel in food preparations. School feeding experiments with kanji (gruel) pudding at Bangalore. *Indian med. Gaz.*, **82**, 143.

DE, S. S. and GANGULY, J. (1947). Heat treatment and the biological value of soyabean protein. *Nature, Lond.*, **159**, 341.

DEAN, R. F. A. (1949). Ein neuer Vorschlag zur Entwicklung der Kinderernährung. *Mschr. Kinderheilk.*, **97**, 471.

DEAN, R. F. A. (1951). Studies of undernutrition Wuppertal 1946–9. 28. The size of the baby at birth and the yield of breast milk. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 275, 346.

DEAN, R. F. A. (1952). The treatment of kwashiorkor with milk and vegetable proteins. *Brit. med. J.*, **ii**, 791.

DEAN, R. F. A. and HOLMAN, W. I. M. (1950). Excretion and intake of B vitamins in newborn infants. *Arch. Dis. Childh.*, **25**, 292.

DESESSARTZ, J. C. (1760). Traité de l'éducation corporelle des enfans en bas âge. J. T. Hérissant, Paris.

DESIKACHAR, H. S. R. and DE, S. S. (1947). Role of inhibitors in soybean. *Science*, **106**, 421.

DESIKACHAR, H. S. R., DE, S. S. and SUBRAHMANYAN, V. (1948a). Studies on the nutritive value of groundnut milk. *Ann. Biochem. exp. Med.*, **8**, 33.

DESIKACHAR, H. S. R., DE, S. S. and SUBRAHMANYAN, V. (1948b). Protein value of soya-bean milk; human feeding experiments. *Indian J. med. Res.*, **36**, 145.

DESIKACHAR, H. S. R. and SUBRAHMANYAN, V. (1949). Infant feeding experiments with soya-bean milk. *Indian J. med. Res.*, **37**, 77.

DEUEL, H. J. Jr., MESERVE, E. R., STRAUB, E., HENDRICK, C. and SCHEER, B. T. (1947). The effect of fat level of the diet on general nutrition. 1. Growth, reproduction and physical capacity of rats receiving diets containing various levels of cottonseed oil or margarine fat *ad libitum*. *J. Nutr.*, **33**, 569.

DE VALLAMBERT, S. (1565). Cinq livres de la manière de nourrir et gouverner les enfans dès leur naissance. Les de Marnesz et Bouchetz frères, Poictiers.

DRAPER, C. I. and EVANS, R. J. (1944). Plant protein concentrates in the chick ration. *Poult. Sci.*, **23**, 507.

EDDY, W. A. and ECKMAN, R. S. (1923). The supplementary protein value of peanut flour. *J. biol. Chem.*, **55**, 119.

EDITORIAL (1865). Baron Liebig's soup for Children. *Lancet*, **i**, 17.

ELMAN, R. (1939). Time factor in retention of nitrogen after intravenous injection of a mixture of amino acids. *Proc. Soc. exp. Biol.*, *N.Y.*, **40**, 484.

ELVEHJEM, C. A. and KREHL, W. H. (1947). Imbalance and dietary interrelationships in nutrition. *J. Amer. med. Ass.*, **135**, 279.

ERSHOFF, B. H. and DEUEL, H. J. Jr. (1944). Inadequacy of lactose and beta-lactose as dietary carbohydrates for the rat. *J. Nutr.*, **28**, 225.

EVANS, R. J. and BUTTS, H. A. (1948). Studies on the heat inactivation of lysine in soy bean oil meal. *J. biol. Chem.*, **175**, 15.

EVANS, R. J. and BUTTS, H. A. (1949a). Inactivation of amino acids by autoclaving. *Science*, **109**, 569.

EVANS, R. J. and BUTTS, H. A. (1949b). Studies on the heat inactivation of methionine in soy bean oil meal. *J. biol. Chem.*, **178**, 543.

EVANS, R. J. and MCGINNIS, J. (1946). The influence of autoclaving soybean oil meal on the availability of cystine and methionine for the chick. *J. Nutr.*, **31**, 449.

EVANS, R. J. and MCGINNIS, J. (1948). Cystine and methionine metabolism by chicks receiving raw or autoclaved soybean oil meal. *J. Nutr.*, **35**, 477.

EVANS, R. J., MCGINNIS, J. and ST. JOHN, J. L. (1947). The influence of autoclaving soyabean oil meal on the digestibility of the proteins. *J. Nutr.*, **33**, 661.

EVERSON, G. J., STEENBOCK, H., CEDERQUIST, D. C. and PARSONS, H. T. (1944). The effect of germination, the stage of maturity and the variety upon the nutritive value of soybean protein. *J. Nutr.*, **27**, 225.

FABER, H. K. and ROBERTS, D. B. (1935). Studies in infantile allergic eczema. 2. Serum lipids, with special reference to saturation of the fatty acids. *J. Pediat.*, **6**, 490.

FAIRBANKS, B. W. and MITCHELL, H. H. (1935). The nutritive value of skim-milk powders, with special reference to the sensitivity of milk proteins to heat. *J. agric. Res.*, **51**, 1107.

FAN, C., WOO, T. T. and CHU, F. (1940). Metabolic studies on the roasted soybean meal as an infant food. *Chin. med. J.*, **58**, 53.

FARBER, S., SHWACHMAN, H. and MADDOCK, C. L. (1943). Pancreatic function and disease in early life. 1. Pancreatic enzyme activity and the coeliac syndrome. *J. clin. Invest.*, **22**, 827.

FINKS, A. J., JONES, D. B. and JOHNS, C. O. (1922). The role of cystine in the dietary properties of the proteins of the cow-pea, *Vigna sinensis*, and of the field pea, *Pisum sativum*. *J. biol. Chem.*, **52**, 403.

FISCHER, A. (1914a). Kuhmilch und vegetabile Milch und ihre Unterschiede in der Magenverdauung besonders mit Rücksicht auf das Problem der Kuhmilch-Intoleranz. *Arch. Verdaukr.*, **20**, 13.

FISCHER, A. (1914b). Neuere Gesichtspunkte für die diätetische Behandlung des Ulcus ventriculi und duodeni, der Hypersekretion, der motorischen Insuffizienz, einiger Stoffwechsel- und Ernährungsstörungen, Herz- und Nierenerkrankungen, mit vegetabiler Milch. *Arch. Verdaukr.*, **20**, 232.

FORBES, E. B., SWIFT, R. W., ELLIOTT, R. F. and JAMES, W. H. (1946). Relation of fat to economy of food utilization. 1. By the growing albino rat. 2. By the mature albino rat. *J. Nutr.*, **31**, 203; 213.

FORBES, E. B., SWIFT, R. W., JAMES, W. H., BRATZLER, J. W. and BLACK, A. (1946). Further experiments on the relation of fat to economy of food utilization. 1. By the growing albino rat. *J. Nutr.*, **32**, 387.

FORBES, E. B., SWIFT, R. W., THACKER, E. J., SMITH, V. F. and FRENCH, C. E. (1946). Further experiments on the relation of fat to economy of food utilization. 2. By the mature albino rat. *J. Nutr.*, **32**, 397.

FRENCH, R. B. and MATTILL, H. A. (1935). The biological value of the proteins of white, whole wheat and rye breads. *Cereal Chem.*, **12**, 365.

FREUDENBERG, E. (1946). Über Säuglingsernährung mit Stutenmilch. *Ann. paediat.*, **166**, 338.

FREUDENBERG, E. (1948). Über Säuglingsernährung mit Stutenmilch. 2. *Ann. paediat.*, **171**, 49.

FRIEDENTHAL, H. (1910). Über die Eigenschaften künstlicher Milchsera und über die Herstellung eines künstlichen Menschenmilchersatzes. *Zbl. Physiol.*, **24**, 687.

FRIEDENTHAL, H. (1914). Ueber Säuglingsernährung nach physiologischen Grundsätzen mit Friedenthal'scher Kindermilch und Gemüsepulvern. *Berl. klin. Wschr.*, **51**, 727.

GALLUP, W. D. (1928). The digestibility of the proteins of some cottonseed products. *J. biol. Chem.*, **76**, 43.

GARDNER, L. I., MACLACHLAN, E. A., PICK, W., TERRY, M. L. and BUTLER, A. M. (1950). Etiologic factors in tetany of newly born infants. *Pediatrics, Springfield*, **5**, 228.

✓ GEIGER, E. (1948). The role of the time factor in feeding supplementary proteins. *J. Nutr.*, **36**, 813.

GEIGER, E. and HAGERTY, E. B. (1949). Growth of rats on hydrolyzed zein. *Arch. Biochem.*, **21**, 239.

GERSTENBERGER, H. J., HASKINS, H. D., MCGREGOR, H. H. and RUH, H. O. (1915). Studies in the adaptation of an artificial food to human milk. *Amer. J. Dis. Child.*, **10**, 249.

GERSTLEY, J. R. (1930). Studies in infant nutrition. 6. Lactose and a maltose-dextrin preparation. *J. Amer. med. Ass.*, **95**, 1233.

GESTEIRA, M. and BAHIA, A. (1932). O leite de coco nos disturbios nutritivos do lactente. *Brazil-med.*, **46**, 173.

GEYER, R. P., BOUTWELL, R. K., ELVEHJEM, C. A. and HART, E. B. (1946). The effect of fat on the utilization of galactose by the albino rat. *J. biol. Chem.*, **162**, 251.

GILLIS, M. B. and NORRIS, L. C., (1949a). Vitamin B_{12} and the requirement of the chick for methylating compounds. *Poult. Sci.*, **28**, 749.

GILLIS, M. B. and NORRIS, L. C. (1949b). The effect of the animal protein factor on the requirement for methylating compounds. *J. biol. Chem.*, **179**, 487.

✓ GILLMAN, J., GILLMAN, T., MANDELSTAM, J. and GILBERT, C. (1945). The production of severe hepatic injury in rats by the prolonged feeding of maize-meal porridge (mealie-pap) and sour milk. *Brit. J. exp. Path.*, **26**, 67.

✓ GOMEZ, F., RAMOS, R., BIENVENU, B. and CRAVIOTO, J. (1950). The recuperation of the under-nourished child using proteins of vegetable and animal origin. *Summaries of Communications, 6th International Congress of Pediatrics, Zürich*, 1950.

✓ GORDON, H. H., LEVINE, S. Z. and MCNAMARA, H. (1947). Feeding of premature infants. A comparison of human and cow's milk. *Amer. J. Dis. Child.*, **73**, 442.

GRAU, C. R. (1946). Protein concentrates as amino acid sources for the chick: corn gluten meal, cottonseed meal and peanut meal. *J. Nutr.*, **32**, 303.

GRAU, C. R. and ALMQUIST, H. J. (1944). Sesame protein in chick diets. *Proc. Soc. exp. Biol., N.Y.*, **57**, 187.

GRAU, C. R. and ALMQUIST, H. J. (1945). Value of sunflower seed protein. *Proc. Soc. exp. Biol., N.Y.*, **60**, 373.

GREAVES, E. O. and MORGAN, A. F. (1933–4). Nutritive value of raw and heated casein with and without added amino-acids. *Proc. Soc. exp. Biol., N.Y.*, **31**, 506.

GREAVES, E. O., MORGAN, A. F. and LOVEEN, M. K. (1938). The effect of amino-acid supplements and of variations in temperature and duration of heating upon the biological value of heated casein. *J. Nutr.*, **16**, 115.

GUY, R. A. (1936). The diets of nursing mothers and young children in Peiping. *Chin. med. J.*, **50**, 434.

GUY, R. A. and YEH, K. S. (1938a). Soybean "milk" as a food for young infants. *Chin. med. J.*, **54**, 1.

GUY, R. A. and YEH, K. S. (1938b). Roasted soybean in infant feeding. *Chin. med. J.*, **54**, 101.

HAM, W. E. and SANDSTEDT, R. M. (1944). A proteolytic inhibiting substance in the extract from unheated soy bean meal. *J. biol. Chem.*, **154**, 505.

- HAM, W. E., SANDSTEDT, R. M. and MUSSEHL, F. E. (1945). The proteolytic inhibiting substance in the extract from unheated soy bean meal and its effect upon growth in chicks. *J. biol. Chem.*, **161**, 635.

HAMILTON, T. S. and NAKAMURA, F. I. (1940). The cystine content of eleven varieties of soybeans. *J. agric. Res.*, **61**, 207.

HANDLER, P. (1947). The biochemical defect underlying the nutritional failure of young rats on diets containing excessive quantities of lactose or galactose. *J. Nutr.*, **33**, 221.

HANSEN, A. E. (1933–4). Serum lipid changes and therapeutic effects of various oils in infantile eczema. *Proc. Soc. exp. Biol., N.Y.*, **31**, 160.

HANSEN, A. E. and BURR, G. O. (1932–3). Iodine numbers of serum lipids in rats fed on fat-free diets. *Proc. Soc. exp. Biol., N.Y.*, **30**, 1201.

HARTMAN, A. M., DRYDEN, L. P. and CARY, C. A. (1949). A role of vitamin B_{12} in the normal mammal. *Arch. Biochem.*, **23**, 165.

HAYWARD, J. W. and HAFNER, F. H. (1941). The supplementary effect of cystine and methionine upon the protein of raw and cooked soybeans as determined with chicks and rats. *Poult. Sci.*, **20**, 139.

✓ HAYWARD, J. W., STEENBOCK, H. and BOHSTEDT, G. (1936a). The effect of heat as used in the extraction of soy bean oil upon the nutritive value of the protein of soy bean meal. *J. Nutr.*, **11**, 219.

HAYWARD, J. W., STEENBOCK, H. and BOHSTEDT, G. (1936b). The effect of cystine and casein supplements upon the nutritive value of the protein of raw and heated soy beans. *J. Nutr.*, **12**, 275.

HEGSTED, D. M., KENT, V., TSONGAS, A. G. and STARE, F. J. (1947). A comparison of the nutritive value of the proteins in mixed diets for dogs, rats and human beings. *J. Lab. clin. Med.*, **32**, 403.

HEGSTED, D. M., TSONGAS, A. G., ABBOTT, D. B. and STARE, F. J. (1946). Protein requirements of adults. *J. Lab. clin. Med.*, **31**, 261.

HENRY, K. M. and KON, S. K. (1946). The supplementary relationships between the proteins of dairy products and those of bread and potato as affected by the method of feeding. With a note on the value of soya bean protein. *J. Dairy Res.*, **14**, 330.

HENRY, K. M. and KON, S. K. (1949). The effect on the biological value of bread nitrogen of additions of dried skim milk and of soya flour. *J. Dairy Res.*, **16**, 53.

HENRY, K. M., KON, S. K., LEA, C. H., SMITH, J. A. B. and WHITE, J. C. D. (1946). Deterioration on storage of dried skim milk. *Nature, Lond.*, **158**, 348.

HENRY, K. M., KON, S. K., LEA, C. H. and WHITE, J. C. D. (1948). Deterioration on storage of dried skim milk. *J. Dairy Res.*, **15**, 292.

HENRY, K. M., KON, S. K. and MAWSON, E. H. (1950). The biological value of the proteins of milk. Section II. C. Human milk. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 269.

HESS, R. (1932). Über milchfreie Ernährung des Ekzemkindes. *Dtsch. med. Wschr.*, **58**, 52.

HESSE, D. (1948). Note préliminaire sur une nouvelle technique de transformation amylasique des amidons crus. *Bull. Acad. nat. Méd.*, **132**, 199.

HILDITCH, T. P. and MEARA, M. L. (1944). Human-milk fat. 1. Component fatty acids. *Biochem. J.*, **38**, 29.

HILL, L. W. (1931). Infantile eczema, with special reference to the use of a milk-free diet. *J. Amer. med. Ass.*, **96**, 1277.

HILL, L. W. and STUART, H. C. (1929). A soy bean food preparation for feeding infants with milk idiosyncrasy. *J. Amer. med. Ass.*, **93**, 985.

HINDES, E. (1926). Milchfreie Diät als Prophylaktikum gegen Ernährungsstörungen im frühen Kindesalter. *Arch. Kinderheilk.*, **78**, 9.

HOFFMAN, W. S. and McNEIL, G. C. (1949). The enhancement of the nutritive value of wheat gluten by supplementation with lysine, as determined from nitrogen balance indices in human subjects. *J. Nutr.*, **38**, 331.

HOLMAN, W. I. M. and DE LANGE, D. J. (1950). Significance of tryptophane in human nicotinic acid metabolism. *Nature, Lond.*, **165**, 112.

HOLMES, A. D. (1920). Digestibility of steam-cooked soy beans and peanuts. *J. Amer. med. Ass.*, **74**, 798.

HOLT, L. E. Jr., TIDWELL, H. C., KIRK, C. M., CROSS, D. M. and NEALE, S. (1935). Studies in fat metabolism. 1. Fat absorption in normal infants. *J. Pediat.*, **6**, 427.

HOPKINS, R. H. and KRAUSE, B. (1937). *Biochemistry applied to malting and brewing.* 2nd impression, 1947. Geo. Allen and Unwin, London.

HORN, M. J., JONES, D. B. and BLUM, A. E. (1950). Methods for microbiological and chemical determinations of essential amino acids in proteins and foods. *Misc. Publ. U.S. Dep. Agric.*, No. 696.

HORVATH, A. A. (1926). Changes in the blood composition of rabbits fed on raw soya beans. *J. biol. Chem.* **68**, 343.

HORVATH, A. A. (1930). Changes in hens' blood produced by a diet of sprouted soybeans. *Amer. J. Physiol.*, **94**, 65.

HORVATH, A. A. (1938–9). The nutritional value of soybeans. *Amer. J. dig. Dis.*, **5**, 177.

HORVATH, A. A. and CHANG, H. (1925). *Trans. 6th triennial Congr. Far Eastern Ass. trop. Med., Tokyo*, 359.

HOU, H. C., RIESEN, W. H. and ELVEHJEM, C. A. (1949). Influence of heating on the liberation of certain amino acids from whole soybeans. *Proc. Soc. exp. Biol., N.Y.*, **70**, 416.

HOVE, E. L., CARPENTER, L. E. and HARREL, C. G. (1945). The nutritive quality of some plant proteins and the supplemental effect of some protein concentrates on patent flour and whole wheat. *Cereal Chem.*, **22**, 287.

HUDSON, N. P. and PARR, L. W. (1924). Relation of reaction of intestinal contents to diet and flora. *J. infect. Dis.*, **34**, 621.

JACQUOT, R. (1944). La farine de tournesol comparée à la farine de soja comme aliment protidique. *Bull. Soc. sci. Hyg. aliment., Paris*, **32**, 80.

JACQUOT, R. and BLAIZOT, J. (1947). Comment doit-on préparer certaines légumineuses "éclatées"? *Bull. Acad. nat. Méd.*, **131**, 524.

JACQUOT, R., MATET, J. and FRIDENSON, O. (1947). Influence de traitements thermiques industriels sur la valeur protidique des aliments. *Ann. Nutr., Paris*, **1**, 157.

JEANS, P. C. (1942). Handbook of nutrition. 19. The feeding of healthy infants and children. *J. Amer. med. Ass.*, **120**, 913.

JOHNS, C. O. and FINKS, A. J. (1920). Studies in nutrition. 2. The role of cystine in nutrition as exemplified by nutrition experiments with the proteins of the navy bean, *Phaseolus vulgaris. J. biol. Chem.*, **41**, 379.

Johnson, D. W. and Palmer, L. S. (1934). The nutritive properties of protein, vitamins B and G, and the germ in rye. *J. agric. Res.*, **49**, 169.

Johnson, L. M., Parsons, H. T. and Steenbock, H. (1939). The effect of heat and solvents on the nutritive value of soybean protein. *J. Nutr.*, **18**, 423.

Jolliffe, N., Tisdall, F. F. and Cannon, P. R. (1950). *Clinical nutrition.* Paul B. Hoeber, New York.

Jones, D. B. (1931). Factors for converting percentages of nitrogen in foods and feeds into percentages of proteins. *Circ. U.S. Dep. Agric.*, No. 183.

Jones, D. B., Caldwell, A. and Widness, K. D. (1948). Comparative growth-promoting values of the proteins of cereal grains. *J. Nutr.*, **35**, 639.

Jones, D. B. and Divine, J. P. (1944). The protein nutritional value of soybean, peanut, and cottonseed flours and their value as supplements to wheat flour. *J. Nutr.*, **28**, 41.

Jones, D. B., Finks, A. J. and Johns, C. O. (1923). Nutritive value of mixtures of proteins from corn and various concentrates. *J. agric. Res.*, **24**, 971.

Jones, D. B. and Murphy, J. C. (1924). Cystine deficiency and vitamin content of the lentil, *Lens esculenta* Moench. *J. biol. Chem.*, **59**, 243.

Jones, D. B. and Waterman, H. C. (1923). Studies on the digestibility of proteins *in vitro*. 4. On the digestibility of the cottonseed globulin and the effect of gossypol upon the peptic-tryptic digestion of proteins. *J. biol. Chem.*, **56**, 501.

Jones, P. E. H. (1951). The absorption of glucose and xylose by adult and newborn rats. *J. Physiol.*, **113**, 276.

Kapfhammer, J. and Habs, H. (1930). Ausnützungsversuche mit Sojaeiweiss und einem neuen Sojaeiweisspräparat an Tier und Mensch. *Dtsch. med. Wschr.*, **56**, 1168.

Karnani, B. T., De, S. S., Subrahmanyan, V. and Cartner, D. (1948). Relative utilization of calcium from soya milk (fortified with di-calcium phosphate) and cow's milk by growing children. *Indian J. med. Res.*, **36**, 355.

Kik, M.C. (1940). The nutritive value of the proteins of rice and its by-products. 2. Effect of amino acid additions on growth. *Cereal Chem.*, **17**, 473.

Kik, M. C. (1941). The nutritive value of the proteins of rice and its by-products. 3. Amino acid content. *Cereal Chem.*, **18**, 349.

Klein, J. (1933). Vegetable milk in infant feeding. *Arch. Pediat.*, **50**, 205.

Klose, A. A. and Fevold, H. L. (1945). Nutritional value of yeast protein to the rat and the chick. *J. Nutr.*, **29**, 412.

Klose, A. A., Greaves, J. D. and Fevold, H. L. (1948). Inadequacy of proteolytic enzyme inhibition as explanation for growth depression by lima bean protein fractions. *Science*, **108**, 88.

Klose, A. A., Hill, B. and Fevold, H. L. (1946). Presence of a growth inhibiting substance in raw soybeans. *Proc. Soc. exp. Biol., N.Y.*, **62**, 10.

Klose, A. A., Hill, B., Greaves, J. D. and Fevold, H. L. (1949). Growth-depressing fractions in raw lima beans. *Arch. Biochem.*, **22**, 215.

Kneen, E. and Sandstedt, R. M. (1943). An amylase inhibitor from certain cereals. *J. Amer. chem. Soc.*, **65**, 1247.

Kon, S. K. (1947–8). A survey of the place of cow's milk in the human diet and of the effect of processing on its nutritive value. *Brit. med. Bull.*, **5**, 170.

Kon, S. K. and Markuze, Z. (1931). The biological values of the proteins of breads baked from rye and wheat flours alone or combined with yeast or soyabean flour. *Biochem. J.*, **25**, 1476.

Kon, S. K. and Mawson, E. H. (1950). Human milk. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 269.

Kuether, C. A. and Myers, V. C. (1948). The nutritive value of cereal proteins in human subjects. *J. Nutr.*, **35**, 651.

Kunitz, M. (1945). Crystallization of a trypsin inhibitor from soybean. *Science*, **101**, 668.

Kunitz, M. (1946). Crystalline soybean trypsin inhibitor. 1. Method of isolation. *J. gen. Physiol.*, **29**, 149.

Kunitz, M. (1947a). Crystalline soybean trypsin inhibitor. 2. General properties. *J. gen. Physiol.*, **30**, 291.

Kunitz, M. (1947b). Isolation of a crystalline protein compound of trypsin and of soybean trypsin-inhibitor. *J. gen. Physiol.*, **30**, 311.

Kunitz, M. and Northrop, J. H. (1936). Isolation from beef pancreas of crystalline trypsinogen, trypsin, a trypsin inhibitor, and an inhibitor-trypsin compound. *J. gen. Physiol.*, **19**, 991.

Lane, D. E. (1931). The nutrition of twins on a vegetable diet during pregnancy, the nursing period and infancy. *Amer. J. Dis. Child.*, **42**, 1384.

Lane, D. E. and Bosshardt, F. H. (1930). Nutrition of children on a mixed and on a vegetable diet. *Amer. J. Dis. Child.*, **40**, 285.

Larsen, I. (1946). Maltavena. The story of a new milk substitute. *Chambers's Journal*, **94**, 661.

Lea, C. H. (1948). The reaction between milk protein and reducing sugar in the "dry" state. *J. Dairy Res.*, **15**, 369.

Lea, C. H. (1950). The role of amino-acids in the deterioration of food: the browning reaction. *Chem. and Ind. (Rev.)*, 155.

LEA, C. H. and HANNAN, R. S. (1950). Biochemical and nutritional significance of the reaction between proteins and reducing sugars. *Nature, Lond.*, **165**, 438.

LESNÉ, E., HESSE, D. and AUGERAU. (1950). Farine maltée suivant une technique nouvelle. Action sur la croissance des enfants hypotrophiques. *Sem. Hôp. Paris*, **26**, 665.

LEWIS, J. H. and TAYLOR, F. H. L. (1947). Comparative utilization of raw and autoclaved soy bean protein by the human. *Proc. Soc. exp. Biol., N.Y.*, **64**, 85.

LIEBIG, J. (1865). Soup for children. *The Popular Science Review*, ed. by Henry Lawson, M.D. **4**, 157. R. Hardwicke, Piccadilly, London.

LIEBIG, J. (1869). On the nutritive value of different sorts of food. *Lancet*, i, 113.

LIGHT, R. F. and FREY, C. N. (1943). The nutritive value of white and whole wheat breads. *Cereal Chem.*, **20**, 645.

LONGENECKER, H. E. (1943). Fats in human nutrition. *J. Amer. diet. Ass.*, **20**, 83.

LUECKE, R. W., McMILLEN, W. N., THORP, F. Jr. and BONIECE, J. R. (1949). The effect of vitamin B_{12} concentrate on the growth of weanling pigs fed corn-soybean diets. *Science*, **110**, 139.

McCANCE, R. A. and SHIPP, H. L. (1933). The chemistry of flesh foods and their losses in cooking. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 187.

McCANCE, R. A. and WIDDOWSON, E. M. (1943). Mineral metabolism of healthy adults on white and brown bread dietaries. *J. Physiol.*, **101**, 44.

McCANCE, R. A. and WIDDOWSON, E. M. (1946). The chemical composition of foods. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 235. 2nd ed.

McCANCE, R. A. and WIDDOWSON, E. M. (1951a). The metabolism of iron during suckling. *J. Physiol.*, **112**, 450.

McCANCE, R. A. and WIDDOWSON, E. M. (1951b). Studies of undernutrition, Wuppertal 1946–9. The German background. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 275.

McCANCE, R. A., WIDDOWSON, E. M. and SHACKLETON, L. R. B. (1936). The nutritive value of fruits, vegetables and nuts. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 213.

McCOLLUM, E. V., ORENT-KEILES, E. and DAY, H. G. (1939). *The newer knowledge of nutrition.* 5th ed. The Macmillan Co., New York.

McCOLLUM, E. V., SIMMONDS, N. and PARSONS, H. T. (1919). Supplementary relationships between the proteins of certain seeds. *J. biol. Chem.*, **37**, 155.

McCOLLUM, E. V., SIMMONDS, N. and PARSONS, H. T. (1921a). Supplementary protein values in foods. 3. The supplementary dietary relations between the proteins of the cereal grains and the potato. *J. biol. Chem.*, **47**, 175.

McCOLLUM, E. V., SIMMONDS, N. and PARSONS, H. T. (1921b). Supplementary protein values in foods. 4. The supplementary relations of cereal grain with cereal grain; legume seed with legume seed; and cereal grain with legume seed; with respect to improvement in the quality of their proteins. *J. biol. Chem.*, **47**, 207.

McCOLLUM, E. V., SIMMONDS, N. and PARSONS, H. T. (1921c). Supplementary protein values in foods. 2. Supplementary dietary relations between animal tissues and cereal and legume seeds. *J. biol. Chem.*, **47**, 139.

McCOLLUM, E. V., SIMMONDS, N. and PITZ, W. (1917). The dietary deficiencies of the white bean, *Phaseolus vulgaris. J. biol. Chem.*, **29**, 521.

McGINNIS, J. and MENZIES, V. H. (1946). Effect of *in vitro* enzymatic digestion of raw soybean flakes on chick growth. *Poult. Sci.*, **25**, 538.

MACKAY, H. M. M. (1940). Soyabean flour with dried milk; a cheap and efficient substitute for breast milk. *Arch. Dis. Childh.*, **15**, 1.

MACY, I. G. (1949). Composition of human colostrum and milk. *Amer. J. Dis. Child.*, **78**, 589.

MANN, R. L. and BRIGGS, D. R. (1950). Effects of solvent and heat treatments on soybean proteins as evidenced by electrophoretic analysis. *Cereal Chem.*, **27**, 258.

MADER, A. (1931). Die Behandlung der Säuglingspyurie mit Soja und ihre Wechselbehandlung. *Klin. Wschr.*, **10**, 2346.

MARAIS, J. S. C. and SMUTS, D. B. (1940a). The biological value of the proteins of maize and maize supplemented with lysine and tryptophane. *Onderstepoort J. vet. Sci.*, **15**, 197.

MARAIS, J. S. C. and SMUTS, D. B. (1940b). The amino acid deficiencies of certain plant proteins and the supplementary effect between plant proteins as measured by means of their biological values. *Onderstepoort J. vet. Sci.*, **15**, 225.

MARAIS, J. S. C. and SMUTS, D. B. (1940c). Further studies on the amino acid deficiencies of plant proteins. *Onderstepoort J. vet. Sci.*, **15**, 387.

MARSHALL, F. (1949). Personal communication. British Diamalt Co., Sawbridgeworth, Herts.

MATET, A., MATET, J. and FRIDENSON, O. (1945). Protides de remplacement et besoins de croissance chez le rat blanc. *Bull. Soc. sci. Hyg. aliment., Paris*, **33**, 10.

MATET, A., MATET, J. and FRIDENSON, O. (1949). Action du DL-α-tocophérol sur la nécrose hépatique du rat provoquée par le soja cru. *C.R. Soc. Biol., Paris*, **143**, 235.

MATET, J., MONTAGNE, R. and FRIDENSON, O. (1947). Unpublished. Quoted by Jacquot, Matet and Fridenson, 1947.

MATHEWS, A. P. (1939). *Physiological chemistry. A text-book for Students.* 6th ed. Wm. Wood and Co., New York.

MAYNARD, L. A., FRONDA, F. M. and CHEN, T. C. (1923). The protein efficiency of combinations of cornmeal and certain other feeding stuffs, notably rice bran. *J. biol. Chem.*, **55**, 145.

MELNICK, D. and OSER, B. L. (1949). The influence of heat-processing on the functional and nutritive properties of protein. *Food Technology*, 3, 57.

MELNICK, D., OSER, B. L. and WEISS, S. (1946). Rate of enzymic digestion of proteins as a factor in nutrition. *Science*, 103, 326.

MEREDITH, H. V. (1935). Measurements of weight and length of boys 2–48 months old. *Univ. Ia Stud. Child. Welf.*, No. 292.

MILLER, B. S., SEIFFE, J. Y., SHELLENBERGER, J. A. and MILLER, G. D. (1950). Amino acid content of various wheat varieties. 1. Cystine, lysine, methionine and glutamic acid. *Cereal Chem.*, 27, 96.

MILLER, J. I. and MORRISON, F. B. (1944). Effect of heat treatment and oil extraction on the utilization and digestibility of soybean protein by lambs. *J. agric. Res.*, 68, 35.

MIRSKY, I. A. (1944). Inhibition of β-hemolytic streptococci fibrinolysin by trypsin inhibitor (antiprotease). *Science*, 100, 198.

MITCHELL, H. H. (1918). The influence of protein feeding on the concentration of amino-acids and their nitrogenous metabolites in the tissues. *J. biol. Chem.*, 36, 501.

MITCHELL, H. H. (1923–4a). The biological value of proteins at different levels of intake. *J. biol. Chem.*, 58, 905.

MITCHELL, H. H. (1923–4b). The supplementary relations among proteins. *J. biol. Chem.*, 58, 923.

MITCHELL, H. H. (1944). Determination of the nutritive value of the proteins of food products. *Industr. Engng Chem. (Anal. Edn)*, 16, 696.

MITCHELL, H. H. (1947). Protein utilization by the adult rat: the lysine requirement. *Arch. Biochem.*, 12, 293.

MITCHELL, H. H. (1948). The biological utilization of proteins and protein requirements. Chapter 2. In *Proteins and amino acids in nutrition*, ed. by M. Sahyun. Reinhold Publishing Corporation, New York.

MITCHELL, H. H. and BEADLES, J. R. (1939). Nutritive value of soybean proteins improved by heating. *Rep. Ill. agric. Exp. Sta.* (1935–1937), p. 93.

MITCHELL, H. H., HAMILTON, T. S. and BEADLES, J. R. (1945). The importance of commercial processing for the protein value of food products. 1. Soybean, coconut and sunflower seed. *J. Nutr.*, 29, 13.

MITCHELL, H. H. and SMUTS, D. B. (1932). The amino acid deficiencies of beef, wheat, corn, oats, and soy beans for growth in the white rat. *J. biol. Chem.*, 95, 263.

MITCHELL, H. H. and VILLEGAS, V. (1923). The nutritive value of the proteins of coconut meal, soy beans, rice bran and corn. *J. Dairy Sci.*, 6, 222.

MITCHELL, H. S. (1935). Cataract in rats fed on galactose. *J. Nutr.*, 9, Proc. 14.

MITCHELL, H. S. (1936). Susceptibility of different strains of rats to nutritional cataract. *J. Nutr.*, 12, 447.

MITCHELL, H. S. and DODGE, W. M. (1935). Cataract in rats fed on high lactose rations. *J. Nutr.*, 9, 37.

MITRA, K. and VERMA, S. K. (1947). The biological value of the proteins of rice, pulse and milk fed in different proportions to human beings. *Indian J. med. Res.*, 35, 23.

MITRA, K., VERMA, S. K. and AHMED, S. (1948). Investigations on biological value of cereal mixtures in a rice eater's diet by human feeding trials. *Indian J. med. Res.*, 36, 261.

MOORJANI, M. N. and SUBRAHMANYAN, V. (1950). Fortification of ground-nut milk with calcium and its availability to albino rats. *Indian J. med. Res.*, 38, 59.

MOORJANI, M. N., SUBRAHMANYAN, V. and SATYANARAYANA, M. C. (1950). Supplementing value of calcium-fortified vegetable milks to a poor South Indian rice diet. *Indian J. med. Res.*, 38, 139.

MORF, H. (1950). Eosinophilic leucemoid. *Guide to Exhibitions, 6th International Congress of Pediatrics, Zürich, 1950.*

MORGAN, A. F. (1931). The effect of heat upon the biological value of cereal proteins and casein. *J. biol. Chem.*, 90, 771.

MORGAN, A. F. and KING, F. B. (1925–6). Changes in biological value of cereal proteins due to heat treatment. *Proc. Soc. exp. Biol., N.Y.*, 23, 353.

MOTTRAM, V. H. and GRAHAM, G. (1948). Hutchison's *Food and the principles of dietetics*. 10th ed. Edward Arnold and Co., London.

MULDER, G. J. (1839). Ueber die Zusammensetzung einiger thierischer Substanzen. *J. prakt. Chem.*, 16, 129.

MÜLLER, E. and SCHLOSS, E. (1914). Die Versuche zur Anpassung der Kuhmilch an die Frauenmilch zu Zwecken der Säuglingsernährung. *Jb. Kinderheilk.*, 80, 42.

MURLIN, J. R., EDWARDS, L. E., HAWLEY, E. E. and CLARK, L. C. (1946). Biological value of proteins in relation to the essential amino acids which they contain. 2. Interconvertibility of biological values illustrated by supplementing egg and soy protein with essential amino acids. *J. Nutr.*, 31, 555.

MURLIN, J. R., NASSET, E. S. and MARSH, M. E. (1938). The egg-replacement value of the proteins of cereal breakfast foods, with a consideration of heat injury. *J. Nutr.*, 16, 249.

MURRAY, H. C. (1948). The biological value of the protein of field pea products with a comparison of several methods used for this determination. *J. Nutr.*, 35, 257.

NEVENS, W. B. (1921). The proteins of cottonseed meal. 2. Nutritive value. *J. Dairy Sci.*, 4, 552.

Northrop, J. H., Kunitz, M. and Herriott, R. M. (1948). *Crystalline enzymes.* 2nd ed. Columbia Univ. Press, New York.

O'Brien, R., Girshick, M. A. and Hunt, E. P. (1941). Body measurements of American boys and girls for garment and pattern construction. *Misc. Publ. U.S. Dep. Agric.*, No. 366. Washington D.C.

Olcott, H. S. and Fontaine, T. D. (1941). The effect of autoclaving on the nutritive value of the proteins in cottonseed meal. *J. Nutr.*, **22**, 431.

✓ Orr, J. B. (1928). *Food, health and income.* Macmillan, London.

Osborne, T. B. and Mendel, L. B. (1914). Amino-acids in nutrition and growth. *J. biol. Chem.*, **17**, 325.

Osborne, T. B. and Mendel, L. B. (1917a). The use of cotton seed as food. *J. biol. Chem.*, **29**, 289.

Osborne, T. B. and Mendel, L. B. (1917b). The use of soy bean as food. *J. biol. Chem.*, **32**, 369.

Osborne, T. B. and Mendel, L. B. (1919). The nutritive value of the wheat kernel and its milling products. *J. biol. Chem.*, **37**, 557.

Parsons, H. T. (1943). Effect of different cooking methods on soybean proteins. *J. Home Econ.*, **35**, 211.

Pasricha, C. W. (1950). Personal communication.   India House, Aldwych, London, W.C.2.

✓ Paterson, D. and Smith, J. F. (1939). *Modern methods of feeding in infancy and childhood.* 7th ed. Constable and Co. London.

Patton, A. R., Hill, E. G. and Foreman, E. M. (1948a). Amino acid impairment in casein heated with glucose. *Science*, **107**, 623.

Patton, A. R., Hill, E. G. and Foreman, E. M. (1948b). The effect of browning on the essential amino acid content of soy globulin. *Science*, **108**, 659.

Platt, B. S. (1936). An approach to the problems of infant nutrition in China. *Chin. med. J.*, **50**, 410.

Platt, B. S. (1945). Tables of representative value of foods commonly used in tropical countries. *Spec. Rep. Ser. med.Res. Coun., Lond.*, No. 253, p. 41.

✓ Platt, B. S. and Moncrieff, A. (1947–8). Nutritional comparison of human and cow's milk for infant-feeding. *Brit. med. Bull.*, **5**, 177.

Polonovski, M. and Lespagnol, A. (1931). Sur deux nouveaux sucres du lait de femme, le gynolactose et l'allolactose. *C.R. Acad. Sci., Paris*, **192**, 1319.

Porter, L. and Carter, W. E. (1942). *Management of the sick infant and child.* 6th ed. The C. V. Mosby Co., St. Louis.

Rapp, K. E., Skinner, J. T. and McHargue, J. S. (1946). The nutritive value of the protein in tobacco-seed oilmeal. *J. Nutr.*, **31**, 261.

Reid, E. (1934). A preliminary report on the preparation of an infant food, a soybean milk-egg powder. *Chin. J. Physiol.*, **8**, 53.

Reid, E. (1935). The nutritive properties of soybean-egg powder, a substitute for cow's milk in infant dietary. *Chin. J. Physiol.*, **9**, 27.

Report of the Scientific Advisory Board (1947). Indian Research Fund Association. Secretariat, New Delhi, India.

Ribadeau-Dumas, L. (1946). Le sevrage du nourrison, l'intolérance au lait et les aliments de remplacement du lait. *Bull. Soc. sci. Hyg. aliment., Paris*, **34**, 56.

Ribadeau-Dumas, L., Mathieu, R. and Willemin, L. (1930). De l'utilisation des protéines végétales dans l'alimentation du nourrisson. *Nourrisson*, **18**, 65. L'aleurone de tournesol. 1. *Nourrisson*, **18**, 161. L'aleurone de tournesol. 2. *Nourrisson*, **18**, 207.

Riesen, W. H., Clandinin, D. R., Elvehjem, C. A. and Cravens, W. W. (1947). Liberation of essential amino acids from raw, properly heated, and overheated soy bean oil meal. *J. biol. Chem.*, **167**, 143.

Rimington, C. (1936). The chemistry of the proteins and amino acids. *Annu Rev. Biochem.*, **5**, 117.

Rittinger, F. R. and Dembo, L. H. (1932). Soy bean (vegetable) milk in infant feeding. *Amer. J. Dis. Child.*, **44**, 1221.

✓ Rittinger, F. R., Dembo, L. H. and Torrey, G. G. (1935). Soy bean (vegetable) milk in infant feeding. Results of three and one-half years' study on the growth and development of 205 infants. *J. Pediat.*, **6**, 517.

Robinson, C. S. and Duncan, E. W. (1931). The effect of lactose and the acid-base value of the diet on the hydrogen ion concentration of the intestinal contents of the rat and their possible influence on calcium absorption. *J. biol. Chem.*, **92**, 435.

Rommel, G. M. and Vedder, E. B. (1915). Beriberi and cottonseed poisoning in pigs. *J. agric. Res.*, **5**, 489.

Rose, W. C. (1938). The nutritive significance of the amino acids. *Physiol. Rev.*, **18**, 109.

Rose, W. C. (1949). Amino acid requirements of man. *Fed. Proc.*, **9**, 546.

Rose, W. C., Haines, W. J. and Johnson, J. E. (1942). The role of the amino acids in human nutrition. *J. biol. Chem.*, **146**, 683.

Rose, W. C., Haines, W. J., Johnson, J. E. and Warner, D. T. (1943). Further experiments on the role of the amino acids in human nutrition. *J. biol. Chem.*, **148**, 457.

Rose, W. C., Oesterling, M. J. and Womack, M. (1948). Comparative growth on diets containing ten and nineteen amino acids, with further observations upon the role of glutamic and aspartic acids. *J. biol. Chem.*, **176**, 753.

Ross-Mackenzie, J. (1935). *Brewing and malting.* 3rd ed. Sir Isaac Pitman and Sons, London.

Rubner, M. (1928). Verdaulichkeit von mit Eiweiss angereichertem Roggenbrot. *Med. Welt.* Sonderdruck No. 1.

Ruhräh, J. (1909). The soy bean in infant feeding. Preliminary report. *Arch. Pediat.,* 26, 496.

Ruhräh, J. (1910). The soy bean as an article of diet for infants. *J. Amer. med. Ass.,* 54, 1664.

Ruhräh, J. (1915). The soy bean and condensed milk in infant feeding. *Amer. J. med. Sci.,* 150, 502.

Russell, W. C., Taylor, M. W., Mehrhof, T. G. and Hirsch, R. R. (1946). The nutritive value of the protein of varieties of legumes and the effect of methionine supplementation. *J. Nutr.,* 32, 313.

Savory, W. S. (1863). Experiments on food; its destination and uses. *Lancet,* i, 381.

Schloss, D. M. (1920). Allergy in infants and children. *Amer. J. Dis. Child.,* 19, 433.

Schroeder, L. J., Cahill, W. M. and Smith, A. H. (1946). The utilization of calcium in soybean products and other calcium sources. *J. Nutr.,* 32, 413.

Scott, M. L. and Norris, L. C. (1949). Studies on the adequacy of human milk and artificial human milk for the rat. *J. Nutr.,* 37, 337.

Scull, C. W. and Rose, W. C. (1930). Arginine metabolism. 1. The relation of the arginine content of the diet to the increments in tissue arginine during growth. *J. biol. Chem.,* 89, 109.

Shohl, A. T. (1939). *Mineral metabolism.* Reinhold Publishing Corp., New York.

Shohl, A. T., Butler, A. M., Blackfan, K. D. and MacLachlan, E. (1939). Nitrogen metabolism during the oral and parenteral administration of the amino acids of hydrolyzed casein. *J. Pediat.,* 15, 469.

Simon, M. and Melnick, D. (1950). The *in vitro* digestibility of raw and heat-processed soy products varying in the nutritive value of the protein. *Cereal Chem.,* 27, 114.

Sinclair, J. F. (1916). Recent observations in the use of soy bean in infant feeding. *N. Y. St. J. Med.,* 16, 83.

Slack, E. B. (1948). Composition of rats fed on diets containing wheat flours of different percentage extraction. *Brit. J. Nutr.,* 2, 214.

Smith, C. A. (1945). *The physiology of the newborn infant.* Charles C. Thomas, Springfield, Ill.

Smith, D. A. and Woodruff, M. F. A. (1951). Deficiency diseases in Japanese prison camps. *Spec. Rep. Ser. med. Res. Coun., Lond.,* No. 274.

Smuts, D. B. and Marais, J. S. C. (1938a). Plant proteins. 3. The supplementary effect amongst certain plant proteins. *Onderstepoort J. vet. Sci.,* 11, 151.

Smuts, D. B. and Marais, J. S. C. (1938b). Plant proteins. 6. The amino acid deficiencies in certain plant proteins. *Onderstepoort J. vet. Sci.,* 11, 407.

Soybean Research Council (1949). Soybean oil and soy protein. *Soybean Digest,* 10, 24.

Spray, C. M. and Widdowson, E. M. (1950). The effect of growth and development on the composition of mammals. *Brit. J. Nutr.,* 4, 332.

Stearns, G. (1933). Soy bean flour in infant feeding. A study of the relation of the comparative intakes of nitrogen, calcium and phosphorus on the excretion and retention of these elements by infants. *Amer. J. Dis. Child.,* 46, 7.

Stearns, G. (1939). The mineral metabolism of normal infants. *Physiol. Rev.,* 19, 415.

Stevens, J. M. and McGinnis, J. (1947). The effect of autoclaving lysine in the presence of carbohydrate on its utilization by the chick. *J. biol. Chem.,* 171, 431.

Stevenson, S. S. (1947). The adequacy of artificial feeding in infancy. *J. Pediat.,* 31, 616.

Stewart, R. A., Hensley, G. W. and Peters, F. N. Jr. (1943). The nutritive value of protein. 1. The effect of processing on oat protein. *J. Nutr.,* 26, 519.

Stoesser, A. V. (1936). Iodine number of serum fatty acids in acute infections of infants with and without eczema. *Proc. Soc. exp. Biol., N.Y.,* 34, 12.

Stoesser, A. V. (1944). Clinical evaluation of soy bean food in eczema of the child. *Ann. Allergy,* 2, 404.

Stoesser, A. V. (1947). Influence of soybean products on the iodine number of the plasma lipids and the course of eczema. *J. Allergy,* 18, 29.

Stokes, J. L., Gunness, M., Dwyer, I. M. and Caswell, M. C. (1947). Heat processing and the availability of lysine in protein. *Nutr. Rev.,* 5, 83.

Subrahmanyan, V. and Sur, B. K. (1949). Supplementary value of lucerne to the poor South Indian rice diet. *Indian J. med. Res.,* 37, 319.

Sumner, E. E. (1938). The biological value of milk and egg protein in young and mature rats. *J. Nutr.,* 16, 129.

Sure, B. (1948). Relative supplementary values of dried food yeasts, soybean flour, peanut meal, dried non-fat milk solids, and dried buttermilk to the proteins in milled white corn meal and milled enriched wheat flour. *J. Nutr.,* 36, 65.

Trowell, H. C. and Dean, R. F. A. (1952). Kwashiorkor. *British Encyclopaedia of Medical Practice, Interim Suppl.* No. 113. Butterworth, London.

Tso, E. (1928). The development of an infant fed eight months on a soybean milk diet. *Chin. J. Physiol.,* 2, 33.

Tso, E. (1929a). A vegetable milk substitute for North China. *Amer. J. Physiol.,* 90, 542.

Tso, E. (1929b). A comparison of the nutritive properties of soybean "milk" and cow's milk. *Chin. J. Physiol.,* 3, 353.

Tso, E. and Chu, F. (1930–1). The nitrogen metabolism in infants on graded intake of soybean "milk" proteins. *Proc. Soc. exp. Biol., N.Y.*, **28**, 218.

Tso, E. and Chu, F. (1931). Nitrogen metabolism in infants on graded intake of soybean "milk" proteins. *Chin. J. Physiol.*, **5**, 287.

Tso, E. and Ling, S. M. (1930–1). Changes in the composition of blood in rabbits fed on raw and cooked soybeans. *Proc. Soc. exp. Biol., N.Y.*, **28**, 219.

Tso, E., Yee, M. and Chen, T. (1928). The nitrogen, calcium and phosphorus metabolism in infants fed on soybean "milk". *Chin. J. Physiol.*, **2**, 409.

Ujsághy, P. (1939). Der Eiweissstoffwechsel des Säuglingsalters im Spiegel des Stickstoff- und Schwefelumsatzes. 1. N- und S-Stoffwechsel gesunder Säuglinge bei natürlicher Ernährung. *Mschr. Kinderheilk.*, **79**, 79.

Ujsághy, P. (1939–40). Der Eiweissstoffwechsel des Säuglingsalters im Spiegel des Stickstoff- und Schwefelumsatzes. 2. N- und S-Stoffwechsel gesunder Säuglinge bei künstlicher Ernährung. 3. N- und S-Stoffwechsel gesunder Säuglinge bei Ernährung mit vegetabilem Eiweiss (Mandelmilch). *Mschr. Kinderheilk.*, **81**, 214; 225.

Underwood, M. (1784). *A treatise on the diseases of children.* J. Mathews, London.

Van Veen, A. G. and Schaefer, G. (1950). The influence of the tempeh fungus on the soya bean. *Docum. neerl. indones. Morb. trop.*, **2**, 270.

Vickery, H. B. (1945). The proteins of plants. *Physiol. Rev.*, **25**, 347.

Voegtlin, C. and Thompson, J. W. (1936). Lysine and malignant growth. 1. The amino acid lysine as a factor controlling the growth rate of a typical neoplasm. *Publ. Hlth Rep. U.S. Treas. Dep., Wash.*, **51**, 1429.

Volz, F. E., Forbes, R. M., Nelson, W. L. and Loosli, J. K. (1945). The effect of soy flour on the nutritive value of the protein of white bread. *J. Nutr.*, **29**, 269.

Von Loesecke, H. W. (1946). Controversial aspects: yeast in human nutrition. *J. Amer. diet. Ass.*, **22**, 485.

Ward-Perkins, B. (1950). Personal communication. Mill House, Thaxted, Essex.

Waterlow, J. C. (1948). Fatty liver disease in infants in the British West Indies. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 263.

Waterman, H. C. and Johns, C. O. (1921). Studies on the digestibility of proteins *in vitro*. 1. The effect of cooking on the digestibility of phaseolin. *J. biol. Chem.*, **46**, 9.

Wergeland, H. (1948). Three fatal cases of probable familial allergy to human milk. *Acta paediat., Stockh.*, **35**, 321.

Westfall, R. J., Bosshardt, D. K. and Barnes, R. H. (1948). Influence of crude trypsin inhibitor on utilization of hydrolyzed protein. *Proc. Soc. exp. Biol., N.Y.*, **68**, 498.

Westfall, R. J. and Hauge, S. M. (1947). The protein efficiency of soybean flour as related to its trypsin inhibitor content. *Fed. Proc.*, **6**, 423.

Westfall, R. J. and Hauge, S. M. (1948). The nutritive quality and the trypsin inhibitor content of soybean flour heated at various temperatures. *J. Nutr.*, **35**, 379.

Wetzel, N. C., Fargo, W. C., Smith, I. H. and Helikson, J. (1949). Growth failure in school children as associated with vitamin B_{12} deficiency. Response to oral therapy. *Science*, **110**, 651.

Widdowson, E. M. (1947). A study of individual children's diets. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 257.

Widdowson, E. M. (1950). Personal communication. Department of Experimental Medicine. Cambridge University.

Wiese, A. C., Petersen, C. F. and Lampman, C. E. (1949). Activity of microbial animal protein factor concentrate in a high energy broiler ration. *Poult. Sci.*, **28**, 752.

Willemin-Clog, L. (1930). *L'emploi des protéines végétales en diététique infantile.* Arnette, Paris.

Williams, C. D. (1933). A nutritional disease of childhood associated with a maize diet. *Arch. Dis. Childh.*, **8**, 423.

Williamson, M. B. (1944). The amino acid composition of human milk proteins. *J. biol. Chem.*, **156**, 47.

Wokes, F. (1946). Malt extract in infant feeding. *Lancet*, ii, 809.

Wolf, P. A. and Corley, R. C. (1939). Significance of amino acids for the maintenance of nitrogen balance in the adult white rat. *Amer. J. Physiol.*, **127**, 589.

Womack, M. and Rose, W. C. (1941). The partial replacement of dietary methionine by cystine for purposes of growth. *J. biol. Chem.*, **141**, 375.

Woods, E., Beeson, W. M. and Bolin, D. W. (1943). Field peas as a source of protein for growth. *J. Nutr.*, **26**, 327.

Woolley, D. W. (1945). Observations on the growth-stimulating action of certain proteins added to protein-free diets compounded with amino acids. *J. biol. Chem.*, **159**, 753.

Woolley, D. W. (1946). Some correlations of growth-promoting powers of proteins with their strepogenin content. *J. biol. Chem.*, **162**, 383.

Work, E. (1948). The amino-acids present in trypsin and the trypsin inhibitor from soya bean. *Biochem. J.*, **42**, xlix.

Young, W. F., Bishop, E. A., Hickman, E. M. and Williams, Y. J. (1949). Protein requirements of infants. 2. Marasmus. *Arch. Dis. Childh.*, **24**, 250.

YUDKIN, A. M. and ARNOLD, C. H. (1934–5). Cataract formation in rats fed on a diet containing galactose. *Proc. Soc. exp. Biol., N.Y.,* **32**, 836.

ZITTLE, C. A. and ELDRED, N. R. (1944). Determination of *l*-lysine with a specific decarboxylase. *J. biol. Chem.,* **156**, 401.

ZUCKER, L. M. and ZUCKER, T. F. (1948). Zoopherin: a nutritional factor for rats associated with animal protein sources. *Arch. Biochem.,* **16**, 115.

ZUCKER, T. F. and ZUCKER, L. (1943). Nutritive value of cotton, peanut, and soy seeds. *Industr. Engng Chem.,* **35**, 868.

ZUCKER, T. F. and ZUCKER, L. M. (1950). "Animal protein factor" and vitamin B_{12} in the nutrition of animals. *Vitam. and Horm.,* **8**, 1.

INDEX